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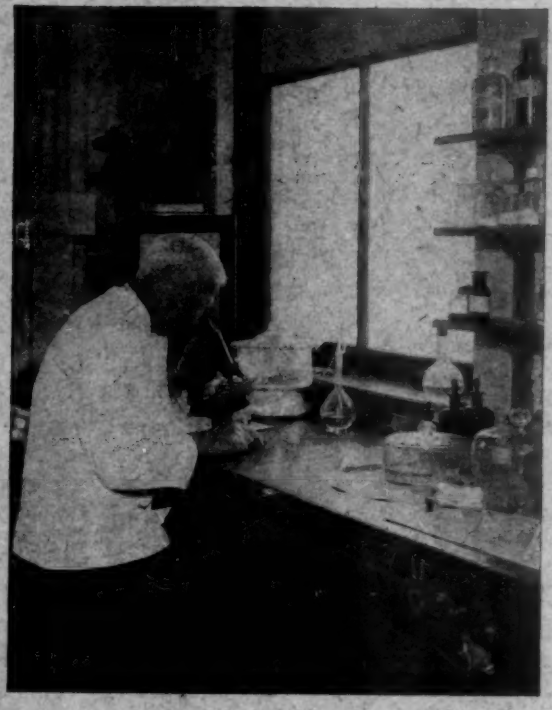

Bio-Chemical Research

Just as the active principle of the suprarenal gland was isolated, it is hoped that, by further researches in the bio-chemical field, the active principles of other ductless glands may be discovered.

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The American Heart Journal

VOL. II FEBRUARY, 1927 No. 3

Original Communications

STUDIES ON THE CIRCULATION

I. EXPERIENCES WITH THE HENDERSON AND HAGGARD METHOD FOR MEASURING THE CIRCULATION*

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IN CLINICAL medicine the need has long been felt for an accurate and practical test to measure the function and reserve of the heart. Since the function of the heart is to maintain an adequate flow of blood, the problem may be shifted to the measurement of the size of the circulation—how large it actually is in relation to what it should be in order to accomplish its task.

The most immediate of the many functions of the circulation is undoubtedly the transport of respiratory gases from source to destination. The volume of this traffic may legitimately be taken as an estimate of the task of the circulation. Defined in this way it is readily measureable under all the varying conditions of rest, nutrition, temperature, disease and work, by well-established methods and in familiar terms. Thus when it has been determined that a subject consumes in a minute 200 c.c. of oxygen under basal conditions and 1000 c.c. while performing 300 kilogram meters of work, the task of the circulation has been measured, for it is virtually stating that every minute a volume of blood must be discharged by the heart, at least sufficient to transport these quantities of oxygen from lungs to tissues.

In estimating, however, the magnitude of the circulation, that is, the minute volume of blood expelled by the heart in order to accomplish the task of transporting the respiratory gases, the clinic certainly has been backward. No practical and reliable clinical method has been available to determine how large the circulation actually is.

The great need and usefulness of such a method, however, will be readily admitted. It might be calculated for example in the case

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referred to, what the minimal circulation must be in order to bring to the tissues the volumes of oxygen consumed. On the basis of 100 per cent hemoglobin and full oxygenation, a liter of arterial blood would take up approximately 200 c.c. of oxygen. This would mean that at rest the minute volume of blood flow must be at least one liter and at work five liters, on the condition that the full load of oxygen that the blood brings to the tissues is released. It is almost certain, however, that under ordinary conditions perhaps not more than a quarter of the oxygen of arterial blood is actually given up to the tissues. The circulation, therefore, must be four times as large, or four liters at rest and twenty liters at work. If a clinical method for actually measuring the circulation were available, it would be possible to determine whether the magnitude of the circulation were equal to the task, that is, whether the found values really reach the values that can be deduced, or whether they exceed or fall short. In this way a sound and quantitative conception of function and reserve could be evolved.

The only fundamental measurements which are at present practical clinically are the rate of the heart, the blood pressure, and the amount of respiratory gases carried by arterial blood. It would be desirable to estimate the equally fundamental value of the volume output of the heart per beat (stroke volume), from which the minute volume of blood flow can be derived (stroke volume × heart rate). Also the exact amount of oxygen the tissues withdraw from arterial blood (arteriovenous difference). When these data are readily determinable, quantitative normal standards could be worked out, as well as criteria of an overactive or failing circulation.

In the past year, as a result of many years of effort to fill the long-felt want, Henderson and Haggard[1] have described a relatively simple method for measuring the circulation in human beings. It is the object of this and ensuing studies to test this method and apply it to the clinical subject in health and a variety of diseased conditions.

Before presenting our experience, it will be profitable to examine the general principle of blood flow determinations and follow its application in this latest method.

Venous blood emerging from different organs varies widely in gaseous content, but in entering the right heart sufficient mixing is effected to enable us to assume the existence of a homogenous venous blood. The "mixed venous blood" therefore is expelled from the right heart into the capillaries of the lungs. There it comes into intimate contact with inspired air on so wide a front as to permit an instantaneous interchange of gases—the blood becoming "arterial," and the air "alveolar." Arterial blood enters the left heart from which it is transmitted without further change through the arterial tree to the tissues. The alveolar air from depths of the lungs is forced out by expiration and becoming mixed with the inspired air remaining in the dead space of the lungs, issues as "expired air."

In 1870 Fick[2] laid down the principle whereby the gases of this system might be employed to measure the minute volume of blood flow.

It will be simpler to proceed from the specific to the general. Let us assume that the mixed venous blood which is only partially reduced, still contained 16 volumes per cent of oxygen, or 160 c.c. oxygen per liter of blood. In becoming arterialized in the lungs, it will take up its full load of oxygen, which we may assume to be 20 volumes per cent or 200 c.c. oxygen per liter of blood. Thus each liter of blood passing through the lungs takes up 40 c.c. of oxygen. This is the arteriovenous oxygen difference. The total amount of oxygen removed by the blood from the inspired air per minute can be derived by subtracting the oxygen content of the air expired from the oxygen content of the air inspired per minute. Let us assume that it is found to be 280 c.c. Since each liter of blood takes up 40 c.c. of this total, it is obvious that 7 liters ($^{280}/_{40}$) of blood have passed through the lungs per minute.

This figure is the expression of the amount of blood expelled by the right heart per minute, and unless we assume a stagnation in the pulmonary circuit, it is also the amount of blood expelled by the left heart per minute.

If the cardiac rate is 70 beats per minute, each ventricle discharges 100 c.c. per beat. In this way the minute volume of blood flow and the stroke volume are determined.

The Fick principle stated in general terms is:

$$\text{Liters blood flow} = \frac{\text{Gas consumption per minute}}{\text{Gas per L arterial blood} - \text{Gas per L mixed venous blood}}$$

Similar deductions may be made from the carbon dioxide of the blood and respiration, or indeed from any freely diffusible gas introduced into the respiratory atmosphere. Thus, nitrogen, ether, nitrous oxide, ethyliodide, etc., have been used. The formula becoming:

$$\text{Liters blood flow} = \frac{CO_2 \text{ production per minute}}{CO_2 \text{ per L mixed venous blood} - CO_2 \text{ per L arterial blood}}$$

Or

$$\text{Liters blood flow} = \frac{\text{Ethyliodide consumption per minute}}{\text{Ethyliodide per L arterial blood} - \text{Ethyliodide per L mixed venous blood}}$$

The practical application of the Fick principle consists in determining the gas consumption per minute and the arteriovenous difference. The minute consumption of the gas employed is determined by the ordinary gasometric methods. The minute volume of respiration is noted on a spirometer from which the subject is breathing. Samples of the inspired and expired air are collected and analyzed for that gas, the difference indicating the amount consumed. The gas content of arterial blood may be determined by direct analysis of a sample of blood obtained by arterial puncture. This procedure is not impractical, although it limits the number of duplicate tests one can perform on the same subject on account of the pain and minor hazards of repeated punctures. Instead of direct blood analysis the gas content of arterial blood may also accurately be determined by analysis of alveolar air, the gases of which are in tension equilibrium with the gases of arterial blood. If the distribution coefficient is known, or the dissociation curves available, it is practical to translate alveolar air concentrations into arterial blood concentrations.*

*Of the distribution coefficient we will speak later. A word about the nature of a dissociation curve will perhaps not be out of place here. Blood by virtue of its content of hemoglobin and buffer systems, has the special property of taking up large quantities of oxygen and CO_2 than can physically dissolve in its fluid volume. It is therefore impossible to say from the ordinary solubility tables how much of these gases blood will take up when it is exposed to definite tensions of these gases. This must be worked out experimentally under the varying conditions of temperature,

In estimating the gas content of mixed venous blood an almost insuperable difficulty in the practical application of the Fick principle in man arises, and explains why until recently it has not been possible to measure the blood flow accurately. Direct puncture of the right heart is of course out of the question. Blood from the arm veins represents local venous blood and not the mixed venous blood of the body as a whole. Plesch[3] in 1909 evolved an indirect way of estimating the gas content of mixed venous blood, from respiratory data. By rebreathing the gas mixture of a small rubber bladder, the gases of that bag finally reach tension equilibrium with the gases of the venous blood which continues to enter the lungs from the right heart. The concentrations of the gases in the final mixture of the rubber bladder may then be determined and employed to calculate the gas content of mixed venous blood from previously established dissociation curves. Or else the subject's blood may be equilibrated with the rebreathed atmosphere, which former, virtually becoming mixed venous blood, may then be directly analyzed for its gas content.

In recent years accurate methods for blood gas analyses have become available so that these general procedures in one form or another have been adopted by Douglas and Haldane,[4] Henderson and Prince,[5] Meakins and Davies,[6] Burwell and Robinson[7] and Field, Bock, Gildea, and Lathrop,[8] who employ them successfully for determinations of blood flow. The method however, for practical clinical use, is too elaborate technically in its delicate blood analyses, blood and gas equilibrations, etc., and suffers the disadvantage of requiring the cooperation of the patient in the respiratory phase of the work.

Since the main difficulty would be eliminated, if we could avoid altogether the correction for mixed venous blood in the computation, other methods with that point in view have been evolved. These accomplish their end by employing a foreign gas instead of the natural oxygen or carbon dioxide. Krogh and Lindhard[9] and their school use nitrous oxide in the atmosphere of the spirometer and permit the subject to breathe for an interval short of the time it takes the blood to return to the right heart, that is, considerably less than a minute. In this case the nitrous oxide of mixed venous blood during the test remains zero and does not enter the calculation of all. But incident to the brevity of the experiment and the intricate respiratory cooperation of the subject, errors requiring large corrections are introduced, resulting in unreliable and uniformly low results. These objections render the method impractical for ordinary clinical use.

Henderson and Haggard[1] also use a foreign gas. In a systematic survey of the possible gases that could be used for this purpose, they hit upon ethyliodide vapor which they claim has the supreme advantage of being practically completely destroyed in the tissues before it returns in the venous blood to the right heart. Thus at a stroke they eliminate the need for estimating the refractory venous element in the Fick principle. The formula becomes now:

$$\text{Liters blood flow} = \frac{\text{Ethyliodide consumption per minute}}{\text{Ethyliodide per L arterial blood} - 0}$$

The method thus consists first in a determination of the amount of ethyliodide absorbed per minute. This is accomplished in the usual way by estimating the difference in ethyliodide between the inspired and expired air. The authors having described an accurate method for analysis of ethyliodide, this phase presents therefor, no difficulties. It remains only to determine the concentration of ethyliodide per liter of arterial blood in order to derive the blood flow. The authors do not

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P_H, electrolyte content, etc. Moreover, the presence of one gas has a marked effect on the amount the blood will take up of the other. The influence of all these factors must therefore be determined on any particular subject's blood, and a chart drawn up, from which one can thereafter read off how much oxygen or CO_2 will be present in blood, if the tension of the gases to which the blood is exposed is known.

employ arterial puncture for this purpose, thereby eliminating completely all blood analysis to the great simplification of their method.*

Instead, they determine the concentration of ethyliodide in a liter of alveolar air and multiply by the distribution coefficient in order to derive the amount per liter of arterial blood. This is a perfectly valid procedure, for in a system of blood and air as exists in the lungs ethyliodide will distribute itself between the two phases in a way which is constant and determinable because it is a property of the gas. The authors have found the coefficient of distribution to be, two. That is to say ethyliodide distributes itself in the proportion of 2 to 1 between the liquid and air phase, and there will always be twice the concentration in arterial blood that exists in alveolar air.

The calculation of the Fick principle then becomes:

$$\text{Liters blood flow per minute} = \frac{\text{Ethyliodide consumption per minute}}{\text{Ethyliodide per L alveolar air} \times 2}$$

OUTLINE OF THE HENDERSON AND HAGGARD APPARATUS AND TECHNIC

A calibrated spirometer, holding about 300 liters, is filled with fresh air. A quantity of ethyliodide having been placed in the bulb of a large pipette, through which the air passes in entering the spirometer, the ethyliodide becomes vaporized and enters the tank where the gases are kept uniformly mixed by an electric fan. The subject's nose is shut off by a spring clip, while he breathes through his mouth in and out of a small respiration box designed by the authors. (Fig. 1.)

The purpose of this box is to keep the inspired and expired air separate. It is divided into two chambers, a lower inspiratory and an upper expiratory, each of about 60 c.c. capacity and communicating by an opening. The inlet of the lower or inspiratory chamber is connected by a large flexible rubber tube to the spirometer and the outlet of the upper or expiratory chamber is connected by another rubber tube to a 4 liter mixing bottle. During inspiration air from the spirometer is drawn into the lower chamber. During expiration the expired air is prevented from flowing back into the spirometer by a rubber flap valve guarding the inlet to the lower chamber. The expired air therefore passes through the upper chamber of the box, through the rubber tube to the mixing bottle, where it is partially trapped. During the following inspiration, the exhaled air filling the expiratory system is prevented from returning to the subject by a second flap valve, guarding the communication between the two chambers. Through special outlets from the spirometer and mixing bottle, samples of inspired and expired air are drawn off for analysis of ethyliodide and a second sample of expired air is analyzed for CO_2 and oxygen. From the latter the oxygen consumption and metabolic rate is readily calculated.

*One of the reasons direct arterial puncture is not employed is that the amount of ethyliodide introduced into the inspired air is so small (about 1:200,000) that the moderate quantity of blood, which might be drawn from an artery for analysis, does not take up enough ethyliodide to permit accurate detection. Hence the alternative use of a large volume of alveolar air.

It should be noted that the expiratory system is in effect a Haldane tube, the proximal portion of which (the upper chamber) after a normal expiration is left filled with air from the depths of the lungs, that is, with alveolar air. The collection of this alveolar air in small portions after each expiration is the most important part of the Henderson

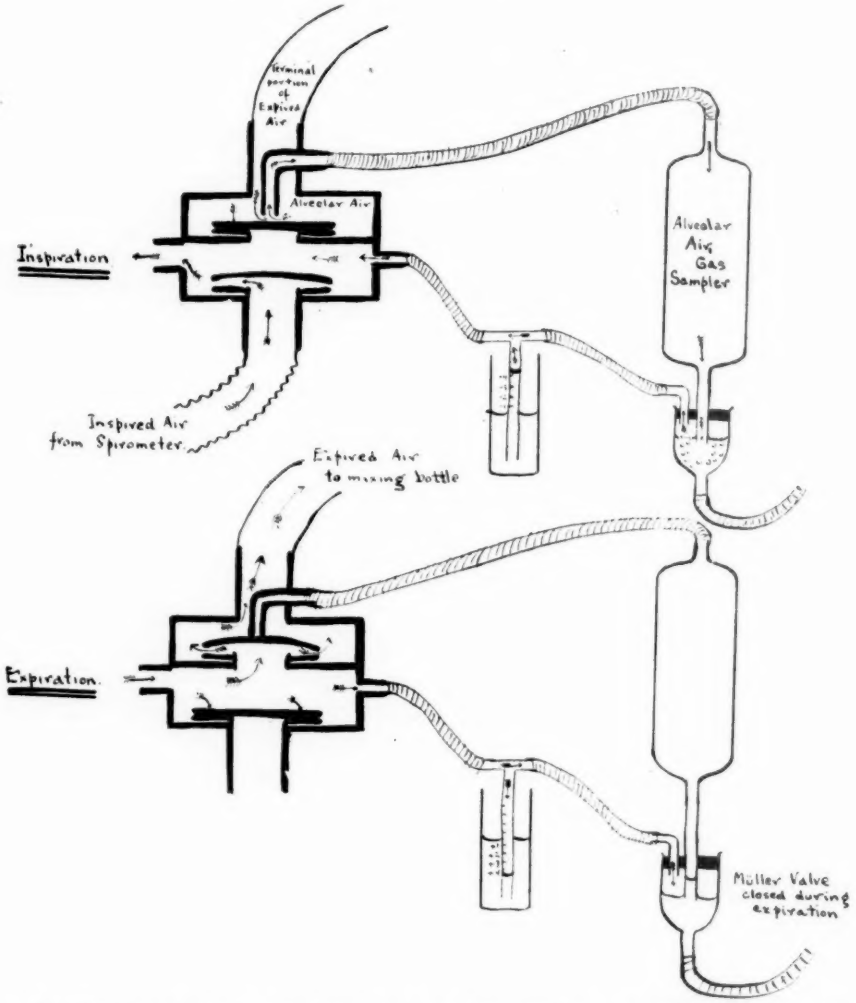

Fig. 1.—Showing action of respiration box and automatic way of collecting alveolar air.

and Haggard technic. This is automatically accomplished by taking advantage of the negative pressure developed in the lower chamber of the respiration box, during inspiration (Fig. 1). By connecting the two chambers through special outlets the inspiratory suction serves to draw a little air out of the upper chamber at the same time that it draws air out of the spirometer. In the secondary circuit thus de-

veloped, is placed a water manometer to gauge the degree of the pressure of the air current and a gas sampler. Thus during each inspiration a jet of alveolar air from the upper chamber is automatically sucked into the gas sampler, which is protected from contamination with the counter-current of expiration by a Müller valve. After ten minutes breathing through the respiration box, about 150 to 200 such jets of air have passed through the gas sampler leaving it thoroughly flushed and filled with alveolar air. It is then removed and anlyzed for ethyliodide.

The gas samplers used for collecting samples of inspired, expired and alveolar air, hold the same volume (0.25 liter) a fact which simplifies the calculation.

$$\text{Minute volume blood flow} = \frac{\text{Ethyliodide consumption per minute}}{\text{Ethyliodide per liter alveolar air x 2}} = \frac{\text{(inspired ethyliodide x 4) - (expired ethyliodide x 4) x liters of respiration per minute}}{\text{(alveolar air ethyliodide x 4) x 2}}$$

It will be seen that the factor 4 cancels out. In other words the actual volume of the gas samplers is of no importance provided all three are the same. If the pulse rate is taken during the experiment, the stroke volume or discharge of the ventricles per beat is derived by dividing the figure into the minute volume of blood flow. As has been stated the minute oxygen consumption is simultaneously calculated from the available oxygen and carbon dioxide analyses of the expired air. If this value is divided by the minute volume of blood flow we derive the amount of oxygen that each liter of blood contributes to the total oxygen consumption. This figure is obviously the arteriovenous oxygen difference.

We have then in this procedure a method of simultaneously measuring the minute volume of blood flow, the volume output of the heart (stroke volume), the oxygen consumption, the arteriovenous oxygen difference, the metabolism, the volume of respiration, etc., on any type of subject without special preparation and with no more of his cooperation than is required in determining the basal metabolism.

CRITICAL ANALYSIS OF THE HENDERSON AND HAGGARD METHOD

The reliability of the above method depends upon four propositions.

(a) That the method for the estimation of ethyliodide in air is accurate.

(b) That the method of obtaining a sample of alveolar air is reliable.

(c) That the distribution coefficient of ethyliodide between air and blood in vivo is two.

(d) That ethyliodide does not return in the venous blood to an appreciable extent.

(a) *The Method of Estimating Ethyliodide.*—With regard to the determination of ethyliodide, the directions of the authors require that the air to be analyzed be passed through a U tube of pure iodide pentoxide kept at a temperature of 160° to 170° C. in an oil bath. The iodine vapor released as a result of the reaction between ethyliodide and hot iodine pentoxide, is caught in an absorption tube containing a solution of potassium iodide. The iodine is estimated by titration with 0.005 N sodium thiosulphate solution. We have been able to obtain consistent results with this method provided the air is passed through the U tube *at a very slow rate.* This point must especially be observed during the first fifteen minutes of the aeration, when the major part of the reaction takes place. We have been unable to collect all the iodine in less than twenty minutes of aeration. But the time may vary according to the way the U tube is packed. If the air current is run through rapidly, the ethyliodide passes through unchanged as is evidenced by the low and variable results. The samples of inspired and expired air were always analyzed by us in duplicate. Table I is a record of the agreement between duplicate analysis in terms of c.c. of 0.005 N sodium thiosulphate. It will be seen that day after day the inspired or spirometer air showed the same concentration of ethyliodide. By daily vaporizing the same quantity of ethyliodide (0.75 c.c.) in an identical volume of air (300 liters) we subjected the analyses to a daily check. The maximal variations it will be seen average

TABLE I

AGREEMENT IN ETHYLIODIDE CONTENT IN TERMS OF C.C. 0.005 N SODIUMTHIOSULPHATE SOLUTION BETWEEN DUPLICATE ANALYSES OF INSPIRED AND EXPIRED AIR

DATE	NAME	INSPIRED AIR			EXPIRED AIR		
		FIRST SAMPLE	SECOND SAMPLE	PER CENT DIFFERENCE	FIRST SAMPLE	SECOND SAMPLE	PER CENT DIFFERENCE
6.4.26	M. R.	3.46	3.56	3.1	1.64	1.58	3.8
6.7.26	L. H.	3.44	3.57	3.8	1.66	1.59	4.2
6.9.26	R. K.	3.82	3.87	1.3	1.78	1.90	6.7
6.10.26	A. F.	3.46	3.49	0.9	1.51	1.55	2.6
6.10.26	E. S.	3.45			1.65	1.69	2.7
6.14.26	J. S.	3.46	3.53	2.0	1.37	1.41	2.9
6.14.26	M. G.	3.38	3.49	3.2	1.68	1.70	1.2
6.17.26	I. M.	3.42	3.46	1.2	1.79	1.90	6.1
6.17.26	Z. W.	3.48	3.44	1.2	1.51	1.57	4.0
6.18.26	L. M.	3.48	3.49	0.3	1.58	1.60	1.3
6.18.26	F. C.	3.49			1.38	1.40	1.4
6.21.26	M. G.	3.46	3.67	6.0	1.65	1.60	3.1
6.21.26	L. M.	3.45	3.63	5.2	1.54	1.68	9.0
6.23.26	A. F.	3.59	3.76	4.7	1.50	1.60	6.6
6.28.26	M. S.*	2.80*	3.00	7.1	1.25	1.14	8.8
6.29.26	I. M.	2.90	3.08	6.2	1.26	1.24	1.6
6.30.26	M. D.	3.05	3.06	0.3	1.23	1.23	0.0
7.1.26	L. L.	2.96	3.01	1.6	1.40	1.44	2.9
Average				3			4.4

*Strength of sodiumthiosulphate solution increased on this date.

less than 4 per cent in 72 consecutive analyses. This seems to us satisfactory for the purpose in view.

Our attempt to check up on the absolute accuracy of the ethyliodide method by calculating the quantity introduced into the tank and comparing with the quantity recoverable, was incomplete. We were unable to determine the influence of factors, such as the proportion of ethyliodide introduced into the tank which dissolves in the water of the spirometer.

An additional control of the reliability of the ethyliodide values found may be derived from a comparison of the pulmonary dead space as calculated from the carbon dioxide of the respiration, and the pulmonary dead space as calculated from the ethyliodide of the respiration. It will be recalled that expired air is a mixture of alveolar air and the inspired air remaining in the dead space of the respiratory system (mouth, trachea, bronchi, bronchioles, etc.). The volume of this dead space is a simple arithmetical derivative from the composition of alveolar air and inspired air, in relation to the final mixture of expired air. Any of the gaseous components may be used in this calculation but all should yield the same result. Thus,

$$\frac{\text{Alveolar } CO_2 - \text{Expired } CO_2}{\text{Alveolar } CO_2 - \text{Inspired } CO_2} = \%\ \text{dead space} = \frac{\text{Alveolar Ethyliodide} - \text{Expired Ethyliodide}}{\text{Alveolar Ethyliodide} - \text{Inspired Ethyliodide}}$$

In the course of the blood flow determinations the composition of the three types of air concerned are determined for CO_2 and ethyliodide. Any gross error entering either during the respiratory period or in the many analyses, would be at once exposed, by a wide disagreement in the ratio derived from the two distinct sets of data. In all our determinations we have calculated the dead space as a means of checking the technical steps. This item will be found recorded in Tables (III, IV, and V) alongside the other critical information.

(b) *The Reliability of the Method for Obtaining Alveolar Air.*—In employing the alveolar air in blood flow determinations, by other methods, the active cooperation of the subject becomes necessary. This is a disadvantage in any clinical method. But Henderson and Haggard have by a very simple device made the process of collecting air from the depths of the lungs, entirely automatic. This device is perhaps the most attractive feature of the method but at the same time, in our opinion, if carelessly employed, the most misleading, in that it exposes the method to a great source of error. The automatic way in which alveolar air is collected, it will be recalled (Fig. 1), consists in trapping a few c.c. of the terminal portion of each *normal expiration* in a gas sampler, so that after ten minutes of normal breathing a sample of air is obtained containing jets of terminal expired air from some 150 to 200 respirations. This is an excellent way of col-

lecting a representative "alveolar air" covering a period of ten minutes. But one may ask at once *is the terminal portion of a normal expiration alveolar air?* On a priori grounds it is doubtful, because as Haldane and Priestley[10] have shown, only the terminal portion of a *forced* expiration is at all constant in gas content and to be regarded as true alveolar air. One may suppose that the terminal portion of a *normal expiration* is still a mixture of alveolar and dead space air. Bearing in mind the purpose to which this alveolar air is to be put, i.e., to derive a value for arterial blood, it becomes imperative to employ only the air which is in contact with arterial blood, that is air coming from the very depths of the lungs.

To test the quality of the "alveolar air" sample collected by the Henderson and Haggard method, the authors themselves suggest analysis of that sample for CO_2. If it is true alveolar air the concentration of CO_2 should be around 5.5 per cent. If it falls unreasonably short of this figure the sample is to be discarded, together with the blood flow figures derived from it. This precaution we have taken in all our determinations and it must be noted that adopting the original technic and apparatus of Henderson and Haggard we were, for a while, unable to obtain samples of true alveolar air. Table II shows some figures for CO_2 on the so-called alveolar air samples of normal subjects, together with the blood flow figures derived from analyses of such samples. It will be seen that the CO_2 values fall far short of the required 5.5 per cent and, in consequence of the failure to obtain true samples

TABLE II

ALVEOLAR CO_2 VALUES ACCORDING TO ORIGINAL AND SLIGHTLY MODIFIED HENDERSON AND HAGGARD TECHNIC

NAME	ORIGINAL METHOD		MODIFIED METHOD		REMARKS
	ALVEOLAR CO_2 PER CENT	BLOOD FLOW LITERS PER MINUTE	ALVEOLAR CO_2 PER CENT	BLOOD FLOW LITERS PER MINUTE	
W. B.	4.7	5.1	5.7	8.8	Normal
W. B.	4.3	5.8			
M. F.	3.8	5.6	5.2	10.1	"
M. F.	3.1		5.0	10.1	
M. K.	5.3	8.9	5.4	10.5	"
M. K.	4.9	5.0	5.7	11.0	
S. W.	4.5	9.9	5.3	8.0	"
S. W.	5.1	7.1	5.3	8.7	
L. M.	4.5	4.3	5.8	7.6	"
L. M.			5.6	7.9	
	4.5		5.4		Average
H. G.	4.7	4.5			Cardiac insufficiency
M. K.	3.4	3.4			Cardiac insufficiency
M. K.	3.8	2.4			
H. L.	4.2	3.7			Mitral stenosis, compensated
P. C.	3.4	4.6			Cardiac insufficiency
E. H.	3.8	1.8			Cardiac insufficiency
	3.9				Average

of air from the depths of the lungs, the blood flow figures vary widely.

This defect became more marked in cardiac subjects (also recorded in Table II). These subjects are at best shallow breathers, barely washing out their pulmonary dead space during a normal respiration. The average value obtained in the normal subjects was as low as 4.5 per cent, while on the cardiac patients it varied around 3.9 per cent.

It is obvious then from a consideration of Table II, that the sample of air we collected and regarded as alveolar air, was in reality a mixture of alveolar air and about 20 per cent or more of dead space air. Two means of corrections suggested themselves. In the first place to diminish the dead space, and secondly to deepen the pulmonary ventilation. Both methods tend to assure air from the depths of the lungs, one by diminishing the dilution and the other by the exhalation of air from deeper parts.

Accordingly we reconstructed the type of respiratory valve box which Henderson and Haggard describe, on a much smaller scale. The original box put out by Arthur Thomas Company according to the author's specifications, contains a dead space of about 120 c.c. In view of the fact that the average tidal air is about 450 c.c., the last quarter of the expired air remains in the valve box. This condition would prevent the collection of the very last part of the expired air. The valve box which we employ in our determinations has a maximal dead space of perhaps less than 20 c.c. so that we are assured of at least one thing, that the air remaining in the upper chamber is really the very last undiluted part of the expired air.

The second step we took toward obtaining a more perfect sample of alveolar air was one suggested by the authors but which we believe they do not carry far enough. It consists chiefly in narrowing down the tube leading from the spirometer to the respiratory valve box to such a degree that a negative pressure of between 3 and 4 cm. of water is created in the lower chamber, during inspiration. The effect of the definite obstruction to inspiration that is in this manner developed, is to lengthen and deepen the inspiration with a consequent, somewhat prolonged and forced expiration. It seems to us that a better washing out of the dead space follows and air from deeper parts of the lungs is left in the expiratory system. Morever, the greater suction during inspiration serves to flush out more completely the alveolar air sampler with jets of terminal expired air, thereby reducing dilution from that source. It may be argued that respiration is rendered somewhat abnormal by this procedure, but this point, which will be discussed later, is perhaps less significant in blood flow measurements than in determining the respiratory exchange. The important thing is to get a good sample of lung air. That these slight modifications of apparatus and technic are effective in producing a better sample of alveolar air, can be

gathered from Table II, which records the alveolar CO_2 and blood flow figures on the same normal subjects who previously gave the low results. It will be seen that the individual values run well over 5 per cent, averaging 5.4 per cent, while the blood flow figures are much higher and more consistent. Indeed, in none of the observations to be subsequently recorded, have we regarded as acceptable, an alveolar CO_2 content that was not well over 5 per cent, and when an analysis showed a value short of this criterion we resorted to comparison with an analysis of alveolar air obtained by the Haldane and Priestley method.[10] This comparison brought out the divergence between the perfect sample of alveolar air and the one we collected on the Henderson and Haggard apparatus. In most cases this divergence was not wide, that is to say, when we obtained a sample of alveolar air low in CO_2 by the Henderson and Haggard method, we found similar low values by the ideal method of obtaining alveolar air, demonstrating that the values we obtained were apparently true for that person. A complete record of the CO_2 values on the alveolar air of our test subjects appears in Tables III, IV and V. It seems to us that before the reliability of a blood flow measurement by this method can be found acceptable, the quality of alveolar air should be determined and recorded alongside the other important analytical information.

(c) *The Distribution Coefficient.*—To determine the distribution coefficient of ethyliodide in a system of air and blood is beyond the scope of this laboratory. Although it would be desirable to have this value confirmed the evidence upon which the authors base their deductions seems sound and abundant. The fact, as we shall later see, that the blood flow figures derived by the use of this factor are of the same order of magnitude as the figures derived by other laboratories working with other applications of the Fick principle supports the correctness of the value. Moreover, for comparative purposes, that is, for comparing the blood flow on normal and abnormal subjects which is the major clinical objective, the exact distribution coefficient is of secondary importance, since a uniform error is introduced.

(d) *Does Ethyliodide Return in the Venous Blood?*—The contention of Henderson and Haggard that ethyliodide is destroyed in the tissues and does not accumulate in the venous blood to an appreciable extent is perhaps the most fundamental proposition upon which the method is based. The evidence upon which it rests is recorded in their paper in four briefly discussed experiments (1, page 212) which in our opinion are not conclusive. The first establishes the fact that on breathing an atmosphere containing ethyliodide, the expired air shows after three minutes, a virtually constant composition for ethyliodide, which persists for eighteen minutes. This point is again demonstrated

TABLE III

DATA ON THE CIRCULATION OF NORMAL MALE SUBJECTS

DATE	NAME	WT.	ALVEOLAR CO_2 PER CENT	PER CENT DEAD SPACE FROM		OXYGEN CONSUMPTION		BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT—PER KILO	ARTERIOVENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD
				CO_2	ETHYL IODIDE	C.C.	ABOVE BASAL RATE PER CENT					
2– 4–26	W. B.	70	5.7	27	28	288	+23	8.8	78	112	1.6	3.3
3–19–26	E. B.	77	5.3	17	23	260	+ 6	7.8	76	104	1.4	3.4
7–15–26	E. B.	75	5.5	21	20	256	+ 5	7.1	75	95	1.3	3.6
3– 9–26	M. E.	65	5.0	25	29	253	+12	7.5	69	108	1.7	3.4
3–31–26	M. E.	65	5.1	19	33	256	+13	6.5	68	96	1.5	4.0
2–15–26	M. F.	71	5.0	22	28	357	+46	10.1	77	131	1.8	3.6
2–10–26	M. F.	71	5.2	32	25	245	− 0	10.1	75	134	1.9	2.4
3–29–26	L. G.	68	5.1	28	22	265	+11	7.2	85	85	1.3	3.7
3–16–26	M. I.	80	5.4	24	24	300	+18	7.7	74	104	1.3	3.9
2–23–26	A. L.	72	5.3	23	27	270	+17	7.2	82	87	1.2	3.8
2–25–26	A. L.	72	5.6	26	28	245	+ 7	6.4	84	75	1.1	3.8
7– 1–26	A. L.	69	5.7	32	31	208	− 9	5.5	79	69	1.0	3.8
3–17–26	M. K.	87	5.7	15	22	362	+38	11.0	87	126	1.4	3.3
3– 2–26	M. K.	87	5.4	19	25	321	+23	10.5	80	132	1.5	3.1
6–21–26	L. M.	65	5.6	30	29	278	+24	7.9	74	106	1.6	3.6
2–18–26	L. M.	65	5.8	31	30	275	+22	7.6	72	105	1.6	3.6
6–24–26	I. M.	66	5.6	24	28	260	+22	7.5	85	89	1.4	3.5
4– 7–26	M. R.	65	6.1	32	27	278	+24	6.9	78	87	1.3	4.0
4– 8–26	M. R.	65	5.6	24	27	282	+25	7.3	83	88	1.4	3.9
6– 4–26	M. R.	65	5.8	33	30	285	+27	7.2	80	89	1.4	4.0
2–11–26	E. R.	78	5.4	32	35	308	+21	8.0	80	100	1.3	3.9
2– 9–26	E. R.	78	5.5		29			9.1	83	110	1.4	
3– 3–26	J. S.	52	5.6	11	16	206	+ 5	7.8	71	109	2.1	2.7
3– 8–26	J. S.	52	5.6	16	17	210	+ 7	9.0	77	117	2.3	2.3
4– 8–26	Y. S.	61	5.1	27	23	289	+30	8.6	80	108	1.8	3.4
4– 9–26	M. W.	65	5.9	15	17	338	+50	9.1	90	101	1.7	3.7
6– 7–26	M. W.	66	6.3	25	20	294	+34	8.3	89	93	1.4	3.6
4– 1–26	W. W.	74	5.3	23	23	314	+23	8.0	86	93	1.3	3.9
4– 2–26	W. W.	74	5.3	23	23	321	+26	8.7	88	98	1.3	3.7
7–16–26	M. R.	65	6.1	27	26	275	+25	8.3	81	102	1.6	3.3
7–23–26	M. R.	65	5.8	26	21	268	+22	9.2	78	118	1.8	2.9
7–26–26	M. R.	65	5.7	23	24	258	+19	8.7	75	115	1.8	3.0
Averages		69	5.55				+22	8.1	78	102	1.5	3.5

TABLE IV

DATA ON THE CIRCULATION OF NORMAL FEMALE SUBJECTS

DATE	NAME	WT.	ALVEOLAR CO_2 PER CENT	PER CENT DEAD SPACE FROM		OXYGEN CONSUMPTION		BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT— PER KILO	ARTERIOVENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD
				CO_2	ETHYL IODIDE	C.C.	ABOVE BASAL RATE PER CENT					
6–18–26	F. C.	51	5.6	20	19	239		6.7	86	79	1.5	3.6
6–30–26	M. D.	60	5.2	28	22	239		8.3	81	102	1.7	2.9
6–10–26	A. F.	48			23	220	+28	6.7	88	76	1.6	3.3
6–23–26	A. F.	48	5.1	27	26	207	+20	6.9	84	82	1.7	3.0
7– 6–26	M. G.	56	5.7	32	32	251	+30	7.3	85	86	1.5	3.5
7–15–26	M. G.	56	5.8	31	29	238	+23	7.9	87	90	1.6	3.0
7–21–26	C. G.	56	5.5	33	30	223		6.3	77	81	1.5	3.6
7–14–26	C. G.	56	5.2	31	31	262	+42	7.5	73	106	1.9	3.5
4–22–26	M. K.	56	5.6	21	23	228	+23	7.1	77	92	1.7	3.2
7–12–26	M. K.	57	5.5	18	20	222	+20	9.5	85	111	2.0	2.3
2–11–26	A. L.	65	5.1	23	22	242	+20	7.8	78	100	1.5	3.1
2–17–26	A. L.	65	4.9	21	31	206	+ 5	8.1	75	108	1.7	2.6
	J. O'S.	47	4.7	33	33	179	− 2	4.8	79	60	1.3	3.8
	J. O'S.	47	4.8	37	30	188	+ 1	4.4	76	58	1.2	4.3
6–28–26	M. S.	60	5.2	27	21	276	+45	7.2	72	100	1.7	3.7
6–14–26	M. S.	60	5.6	27	23	231	+17	7.1	81	88	1.5	3.3
4–23–26	E. S.	55	4.7	28	29	220	+18	6.7	67	100	1.8	3.3
4–10–26	E. S.	55	4.8	32	33	196	+ 6	6.7	72	92	1.7	2.9
6–16–26	O. U.	48	5.3	25	27	300		7.0	79	88	1.8	4.3
6–17–26	Z. W.	55	5.4	27	26	217		5.2	73	71	1.3	4.2
7–19–26	M. N.	66	5.6	24	25	236	+26	8.6	82	105	1.6	2.9
9–15–26	M. N.	64	5.7	18	21	251	+17	9.5	81	117	1.8	2.7
9–20–26	M. B.	54	6.1	21	19	209	+12	7.4	82	94	1.7	2.9
9–20–26	M. B.	54	6.1	20	21	226	+20	7.4	85	87	1.6	3.1
7–29–26	J. S.	53	5.1	31	33	210	+12	6.7	78	86	1.6	3.1
9–26–26	M. B.	65	6.2	32	31	281	+40	8.8	76	116	1.8	3.2
9–23–26	M. B.	64	6.1	33	31	286	+43	9.5	76	125	2.0	3.0
Averages		56	5.4					7.3	79	93	1.64	3.3

in experiment 3. The finding would seem to indicate that the body does not gradually become saturated with ethyliodide, resulting in an increasing return in the venous blood and eventually in the expired air. What then is the fate of the ethyliodide? The fourth experiment supplies the answer. After inhaling air containing ethyliodide until over 2242 units of ethyliodide were absorbed, fresh air breathing was resumed and the expired air collected for nine minutes. In the first minute (eight liters of expired air) twenty-four units of ethyliodide were recovered; in the next three minutes (twenty-four liters expired air) twelve units ethyliodide were recoverd; and in the last five minutes (40 liters of expired air) no ethyliodide at all could be detected. In other words, less than 2 per cent of the amount of ethyliodide absorbed was recovered. Apparently the rest was destroyed. The third experiment brings out the same fact. In only one experiment (number 2) is an attempt made to estimate directly the concentration of ethyliodide returning in venous blood. After breathing air containing ethyliodide for three minutes until 1200 units were absorbed, the subject rebreathed for one minute the air of a two liter rubber bag. This procedure, as we have seen, gives a sample of venous pulmonary air, from which the concentration in venous blood can be derived by employing the distribution coefficient. They found three units of ethyliodide per liter of venous pulmonary air, whereas if no ethyliodide had been destroyed 7.5 units would have appeared. A 40 per cent return in the venous blood is therefore indicated. The authors make no comment on this critical experiment, which would seem to refute their contention.

We attempted to repeat their experiments in order to throw further light on this important point. In all our blood flow determinations we collected samples of the expired air in duplicate between the sixth and twelfth minutes after the beginning of ethyliodide inhalation. We invariably found the concentration of ethyliodide to be constant within .3 to 4.5 per cent, thereby confirming the first demonstration of Henderson and Haggard. We were able also to confirm the fact that, after a period of ethyliodide inhalation, less than 2 per cent of the total amount absorbed could be recovered in the subsequent expirations. In directly estimating the concentration of ethyliodide returning in venous blood we performed two experiments. In the first, after breathing air containing ethyliodide for ten minutes until 433 units were absorbed the subject washed out his lungs by deeply breathing room air for one minute, and then he was allowed to rebreathe from a two liter bag, for one minute. The venous pulmonary air was found to contain 0.4 units per liter, whereas if no ethyliodide had been destroyed we should have recovered 3.8 units. This represents a return of 12.5 per cent. In the second experiment similarly carried out until 400 units had been absorbed, rebreathed samples of air were

TABLE V

DATE	NAME	WT.	ALVEOLAR CO_2 PER CENT	PER CENT DEAD SPACE FROM		OXYGEN CONSUMPTION		BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KILO.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
				CO_2	ETHYL IODIDE	C.C.	ABOVE BASAL RATE PER CENT						
2–17–26	H. G.	68	5.5	31	31	286	+26	6.1	94	65	.96	4.7	Male, age fifty-four. Hypertension, cardiac insufficiency, auricular fibrillation, ambulant.
2–19–26	H. G.		5.8	31	26	308	+35	5.9	95	62	.91	5.3	
2–16–26	H. G.		5.5	22	33	301	+33	6.3	109	58	.85	4.7	
3–11–26	S. W.	53	5.0	46	43	223	+27	3.1	91	34	.64	7.2	Female, age fifty-seven. Hypertension, cardiac insufficiency, regular, semiambulant.
3–11–26	S. W.		4.6	42	36	251	+43	4.3	94	46	.80	5.9	
3–19–26	H. W.	45	5.4	38	35	264	+22	5.3	91	58	1.29	5.0	Male, age fifteen. Rheumatic valvular disease. Aortic insufficiency, mitral stenosis, compensated, palpitation major symptom, regular, semiambulant.
3– 5–26	H. W.		5.5	37	37	250	+15	4.8	98	49	1.02	5.3	
3– 3–26	H. W.		5.4	40	40	319	+52	6.2	109	57	1.23	5.2	
3–22–26	M. W.	48	5.1	33	40	248	+33	4.7	97	48	1.00	5.3	Female, age fifteen. Rheumatic valvular disease, mitral stenosis, compensated, dyspnea major symptom, semiambulant.
3–15–26	M. W.		5.1	32	33	238	+28	5.1	107	48	1.00	4.6	
4– 2–26	F. H.	58	5.2	41	48	301	+59	4.4	89	50	.86	6.8	Male, age sixty-five. Hypertension, cardiac insufficiency, auricular fibrillation, bed patient.
3–12–26	P. W.	39	5.0	38	29	185	+23	3.5	100	35	.92	5.3	Female, age twenty-five. Rheumatic valvular disease, mitral stenosis and aortic insufficiency. Cardiac insufficiency, auricular fibrillation. Bed patient.
3–16–26	P. W.		5.1	40	34	153	+ 2	2.8	92	30	.78	5.4	

TABLE V—CONT'D

DATE	NAME	WT.	ALVEOLAR CO_2 PER CENT	PER CENT DEAD SPACE FROM		OXYGEN CONSUMPTION		BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KILO.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
				CO_2	ETHYL IODIDE	C.C.	ABOVE BASAL RATE PER CENT						
3–24–26	B. N.	49	5.0	29	30	223	+31	3.4	66	52	1.00	6.9	Female, age thirty-six. Rheumatic valvular disease. Mitral stenosis and insufficiency. Aortic insufficiency. Cardiac insufficiency, auricular fibrillation. Bed patient.
3–31–26	B. N.		5.3	28	31	215	+27	4.4	70	63	1.28	5.0	
4– 1–26	M. G.	69	4.1	27	29	299	+41	4.9	83	60	.86	6.1	Male, age thirty-six. Rheumatic valvular disease, mitral stenosis and insufficiency, compensated. Hemiplegia major symptom, regular, ambulant.
3– 8–26	M. G.		4.2	30	40	266	+26	5.1	87	58	.91	5.3	
3–20–26	M. G.		4.5	35	31	271	+28	5.4	87	63	.98	5.0	
4– 5–26	L. H.	38	5.2	24	24	197	+30	3.9	89	44	1.14	5.1	Female, age twenty-four. Rheumatic valvular disease. Mitral stenosis and insufficiency, cardiac insufficiency, auricular fibrillation. Bed patient.
11–17–25	L. M.	55	5.1	29	27	240	+15	4.4	100/85	44	.81	5.4	Male, age sixty-one. Diabetes. Hypertension, cardiac insufficiency, auricular fibrillation, semiambulant.
11–24–25	E. B.	100	5.0	25	26	381	+46	7.9	87	90	.90	4.8	Female, age sixty-five. Obesity. Hypertension, cardiac insufficiency, regular, ambulant.
Averages			5.1				+31	4.9	91	54	.96	5.5	

taken at intervals of four minutes. After one minute the pulmonary venous air contained 0.24 units, after thirteen minutes, 0.08 units. In the event of no destruction, the venous pulmonary air would have contained three units, indicating a maximum return of 8 per cent in the venous blood which after thirteen minutes fell to 2.6 per cent. A venous return of 10 per cent seems therefore probable.

TECHNICAL EXPERIENCE WITH THE HENDERSON AND HAGGARD METHOD

In the determinations to be reported in the following pages we were less concerned with working out standard values on normal or diseased subjects than with feeling out the method to satisfy ourselves on the point of its clinical reliability. As a result most of our efforts were directed toward standardizing technic and discovering the sources of error. Our confidence in the ability of this method to yield consistent results has steadily grown, especially if reasonable attention is given to the technical points where error is most likely to enter. It is necessary to give some of these more detailed discussion.

The ethyliodide used was the ordinary market product which we purified and redistilled. This procedure yielded a colorless oily liquid with a B.P. of 72 degrees. In vaporizing this substance in the spirometer we invariably pipetted out the same quantity and mixed it in the same total volume of air. This constant technic, as has been said, affords a daily check on the analyses of ethyliodide for it should be possible to find the same daily concentration (within 5 per cent) in the tank air. By using only 0.7 c.c. of ethyliodide, the inspired air is so dilute a mixture of this gas that its odor is only barely detectable. Few subjects complained of the slight ethereal odor. After the first few breaths it was forgotten. When we omitted to warn the subject that the atmosphere would be "slightly stuffy," it wasn't noticed at all. Some subjects were left with a slight rawness of the throat coming on in about an hour, but which disappeared after several hours.

We always permitted the fan of the spirometer to run for fifteen minutes before regarding the gases as thoroughly mixed, and repeated analyses of the lower and upper strata of tank air proved the uniformity of the mixture after this interval. During these minutes the subject was resting by way of preparation, or was having the respiration valve box adjusted.

In adjusting the valve box to the subject, we avoided strained positions. We adopted the upright sitting posture as the one of choice. This was made necessary in view of the influence of posture on blood flow as Field and Bock[11] have shown, and especially since we wished to compare normal with cardiac subjects who were usually in the orthopneic position. Before throwing the tank into the respiratory circuit, the inlet tube was narrowed by a screw clamp until the nega-

tive pressure on the water manometer read −3 to −4 cm. during inspiration. Our normal subjects did not find breathing through this constriction noticeably uncomfortable. With dyspneic patients, encouragement, coaching and patience were usually necessary. We failed only with those patients who were markedly gasping for breath. And it may be observed that this is the group where decompensation is so advanced that blood flow determinations are of secondary interest.

Most of the experimental periods lasted ten minutes. If a single operator ran the test it was often impossible to finish all that was to be done in this time. We preferred to count the pulse frequently because in some subjects it rose from 5 to 10 beats per minute during the test. This was especially desirable in cardiacs with irregular hearts or tendency to tachycardia. Hence a second operator was frequently necessary. Duplicate samples of inspired air could be drawn off at any time during the run but samples of expired air were better taken after thirty-five to forty liters had been breathed, to allow the mixing bottle to become thoroughly flushed with expired air.

The gas analyzer employed was the Henderson modification of the Orsatt apparatus which yielded a fresh air analysis for O_2 plus CO_2 averaging 21.10 per cent for 63 analyses during eight months. With this analyzer we were able to obtain very satisfactory basal oxygen consumption figures. It was only necessary to adopt a standard time for the burette drainage (such as one and one-half minutes) controlled by a stop watch, to get consistent readings.

Complete gas analyses including O_2 and CO_2 in expired air, CO_2 on the alveolar air, and CO_2 on the alveolar air collected by the Haldane method, were usually completed within half an hour. These were done simultaneously with the ethyliodide determinations so that there was no additional time expenditure.

The analysis of the samples for ethyliodide have already been discussed. It need only be said that we found the standardization of every step of that analysis paid with a reward of greater accuracy and consistence. The length of aeration was timed and the speed roughly standardized. The potassium iodide solution was of uniform strength. The total volume of the titration solution kept constant and its P_H roughly controlled. The starch solution was uniformly prepared. The thiosulphate solution was accurately standardized. The titration burette was of the most accurate calibration and readings were made to one hundredth of a c.c. These precautions may seem superfluous in making comparative titrations. This is in part true with regard to the determinations of the iodine in the inspired and expired air samples, where a tenth of a c.c. in titration makes only a small error. But in the analysis of the iodine in the alveolar air sample which is the determination upon which the accuracy of the whole method depends, a difference of a single drop in the titration makes

an error of 5 per cent in the blood flow determination. Moreover, we are dealing with a very dilute iodine solution of which the end-point is none too sharp. It will be seen therefore that in this latter analysis, one cannot be too finical. It was our practice to run a blank aeration of ten minutes on the iodine pentoxide tube before and after each gas sampler analysis. On the samplers containing the higher concentration of ethyliodide a residue of 10 per cent or less was usually recovered. These controls stretched the analysis over a period of two hours, making the complete blood flow determination in our hands an operation requiring two and a half hours to perform by a single operator. It should be noted, however, that the time of operation might be much reduced by employing several pentoxide tubes for the simultaneous aeration of the three samples.

BLOOD FLOW DETERMINATIONS ON NORMAL AND CARDIAC SUBJECTS

Our subjects were of two groups: normals, comprising healthy young adults chosen from among the medical and nursing staffs, and a group of miscellaneous cardiac patients. Our primary interest, as has been said, lay in the method, so that only a passing attempt will be made to interpret data obtained from the clinical standpoint.

In Table III are recorded thirty-two observations on seventeen normal male subjects. In only a few cases was the measurement of the circulation made under basal metabolic conditions. Since the metabolic level was simultaneously determined, incidental to the measurement of the oxygen consumption, it is possible to relate the blood flow figures to the metabolism of the period. The subjects were taken in the afternoon or morning usually after a light breakfast or lunch and several hours of moderate activity. They were rested in the sitting position for at least fifteen minutes before the experiment began.

In Table IV will be found a group of twenty-seven observations on sixteen normal female subjects.

In Table V are tabulated twenty-one observations on eleven miscellaneous cardiac patients, the specific clinical information being given with each case.

The thirty-two observations on seventeen adult male subjects yielded an average minute volume of blood flow of 8.1 liters. The average pulse was 78, so that the stroke volume or discharge of each ventricle per beat was 102 c.c. In only one subject was the stroke volume below 85 c.c., the others ranging between 85 c.c. and 130 c.c.

Henderson has pointed out[12] that the stroke volume is probably a function of the body weight and that the stroke index (stroke volume divided by body weight in kilos) or volume of blood per kilo per beat is a reasonably constant unit. In our series the average stroke index was 1.5 c.c., with an average deviation for the thirty-two observations of ± 0.24 c.c. or ± 16 per cent.

The arteriovenous oxygen difference in our series averaged 3.5 c.c. per 100 c.c. of blood, with an average deviation for thirty-two observations of ±0.35 c.c. or ±10 per cent. These observations it will be noticed were not made under basal conditions but under an average oxygen consumption of plus 22 per cent, using the standard tables.

As far as the value of the a-v oxygen difference goes, however, this condition is of probably minor significance. Since, as Henderson has shown, the blood flow is a function of the oxygen consumption, both would vary more or less proportionately, leaving the quotient, which is the a-v oxygen difference, changed only insignificantly.

In twenty-seven observations on sixteen young female adults the average minute volume of blood flow was 7.3 liters. The average pulse was 78, yielding a stroke volume of 93 c.c. per beat for each ventricle. This value is about 10 per cent smaller than in the male subjects. But in view of the 20 per cent smaller average weight of the female series, the stroke index is 10 per cent higher. Thus the volume of blood per kilo per beat is 1.64 c.c., with an average deviation of ±0.15 c.c. or ±9 per cent. The arteriovenous oxygen difference as might be anticipated was close to the value found in male subjects, that is, 3.3 c.c. per 100 c.c. of blood, with an average deviation of ±0.4 c.c. or ±12 per cent.

On the small group of miscellaneous cardiac patients we made twenty-one observations on eleven cases. The average minute volume of blood flow was 4.9 liters and the average pulse was 91, giving a stroke volume of 54 c.c. per beat. This value is more than 40 per cent below those found on our healthy adults. Of even greater significance is the fact that the highest figures of the cardiac group were well below the lowest figures of the normal groups. The stroke index averaged 0.96 c.c. per kilo per beat, with practically all the values below 1.2 c.c., as compared with the normal subjects in whom all the values were above 1.2 c.c. The average arteriovenous oxygen difference was 5.5 c.c. per 100 c.c. blood. It is significant that all the values were greater than 4 c.c., whereas among the normal cases over 90 per cent had an a-v oxygen difference less than 4 c.c.

DISCUSSION

In coming to a decision regarding the accuracy and usefulness of a clinical quantitative method it is necessary to take into consideration not only the consistency of the results but the degree of "absolute" accuracy attainable (in so far as we may speak of a biological method as absolutely accurate). On the score of the former, the Henderson and Haggard method, as we shall see in Table VI, gives abundant proof of its worth. With regard to the second consideration, we believe we are in a position to estimate within reasonable limits how

TABLE VI

NORMAL MALE SUBJECTS				NORMAL FEMALE SUBJECTS				CARDIAC SUBJECTS			
NAME	STROKE VOLUME	AVERAGE	PER CENT DEVIATION FROM AVERAGE	NAME	STROKE VOLUME	AVERAGE	PER CENT DEVIATION FROM AVERAGE	NAME	STROKE VOLUME	AVERAGE	PER CENT DEVIATION FROM AVERAGE
E. B.	104		4.0	A. F.	76		3.8	H. G.	65		4.8
	95	100	5.0		82	79	3.8		62	62	0.0
M. E.	108		5.9						58		6.4
	96	102	5.9	M. G.	86		2.3	S. W.	34		15.0
M. F.	131		1.5		90	88	2.3		46	40	15.0
	134	133	0.8	C. G.	81		13.8	H. W.	58		5.5
A. L.	87		13.0		106	94	12.8		49	55	10.9
	75	77	2.6	M. K.	92		9.8		57		3.4
	69		10.4		111	102	8.8	M. W.	48		0.0
M. K.	126		2.3	A. L.	100		3.8		48	48	0.0
	132	129	2.3		108	104	3.8	P. W.	35		6.0
L. M.	106		0.0	J. O'S.	60		1.7		30	33	9.1
	105	106	0.9		58	59	1.7	B. N.	52		10.4
M. R.	87		1.1	M. S.	100		6.4		63	58	8.6
	88	88	0.0		88	94	6.4	M. G.	60		0.0
	89		1.1	E. S.	100		4.2		58	60	3.3
E. R.	100		5.0		92	96	4.2		63		5.0
	110	105	5.0	M. W.	105		5.4	H. L.	86		2.4
J. S.	109		3.5		117	111	5.4		82	84	2.4
	117	113	3.5	M. B.	94		3.3	Average per cent deviation			5.7
M. W.	101		6.2		87	91	4.4				
	93	97	6.2	M. I. B.	116		4.1				
W. W.	93		3.1		125	121	3.3				
	98	96	2.1	Average per cent deviation			5.2				
M. R.	102		8.9								
	118	112	5.3								
	115		2.7								
Average per cent deviation			3.8								
Total average per cent deviation											4.9

closely the method approaches complete accuracy by taking into account the recognizable inherent errors.

It would appear that there are two definitely uncertain elements. The return of a portion of the ethyliodide in the venous blood and the method of collecting the sample of alveolar air. Our own work would seem to indicate that by the end of a ten minute inhalation experiment about 10 per cent of the total amount of ethyliodide absorbed is still present undestroyed in venous blood. In our calculations we have ignored this error, possibly rendering our results thereby too low by 10 per cent. But is such a venous return present from the start of the experiment or does it represent the final accumulation after ten minutes inhalation? If the latter were true the error introduced in ignoring this factor may be reduced to smaller and negligible proportions. This is not an easy point to settle experimentally. From the fact already established that the expired ethyliodide is constant from the first few minutes, it would appear that a slow accumulation does not take place and this error present at the end of the experiment was probably a factor throughout.

The other uncertain element in the Henderson and Haggard method also tends to produce low results. Thus, if the sample of alveolar air collected is not really from the depths of the lungs, the content of ethyliodide would naturally be too high, yielding a higher figure for the ethyliodide of arterial blood, and hence a smaller blood flow. But in our opinion this source of error, which is a constant threat in the Henderson and Haggard method, can be practically eliminated. As has been pointed out the value for the CO_2 content of alveolar air is the best indication of the degree to which this factor is influencing the results. It will be seen from our series that in the normal subjects (Tables III and IV) the CO_2 values averaged 5.5 per cent in males and 5.4 per cent in females. Certainly we are dealing with true alveolar air. In only three of the thirty-three cases were the values obviously low. It must be admitted here that, in a certain number of people, it will be impossible to determine the blood flow by the Henderson and Haggard method because of this difficulty, but in our opinion the number is small. Even in the cardiac subjects (Table V) it will be seen that it is possible to obtain good samples of alveolar air. In view of the recognized diminution in CO_2 tension that obtains in the alveolar air of decompensated cardiac cases, our average of 5.1 per cent indicates results as acceptable as in the normal subjects. But here too, a certain proportion of failures will doubtless be encountered, although our series is too small to give a more precise estimate.

These two sources of error then, if they enter at all, influence the results in the same direction, that is, toward values too low by 10 per

cent or possibly more. The validity of this deduction might be tested by comparing our results with those obtained by other methods.

Field, Bock, Gildea and Lathrop, working with the Fick principle and using CO_2 as the gas, have published forty observations on twenty-one normal subjects under basal conditions. Their average minute volume of blood flow is 7.4 liters with a stroke volume of 120 c.c. and a stroke index of 1.74. Our own series of sixty observations on thirty-three normal subjects compares very closely with theirs. Thus, our average minute volume of blood flow was 7.7 liters, with a stroke volume of 98 c.c. and a stroke index of 1.57. The last two figures seem to bear out the deduction that the Henderson and Haggard method gives values too low by 10 per cent or more. It must be noted, however, that the conditions under which the two sets of observations were made were such as to yield higher values by the Field, Bock, Gildea and Lathrop method. Their determinations were made under basal conditions and subjects lying flat; ours, on the other hand, were taken on a somewhat elevated metabolic level but subjects sitting up. As Field and Bock have themselves shown, the blood flow in the lying position is about 25 per cent higher than in the sitting posture, a difference which is partly annulled by the elevated metabolic level of our subjects. When due allowance is made for this factor it will be seen that our values are practically identical with theirs.

If the Henderson and Haggard method then gives results that are of the same order of magnitude as other methods, what becomes of the inherent errors? One of two explanations must be admitted. Either the theoretical error is negligible in practice or other errors enter in the course of the method which neutralize the first. It is difficult to see from where such errors in the opposite direction would arise.*

Moreover, if the accuracy of the Henderson and Haggard method depended upon a counteralignment of errors, it would certainly show little tendency to constancy. The dependability of the method is, on the contrary, amply demonstrated in Table VI. Here we have gathered sixty-eight duplicate or triplicate determinations of the stroke volume on thirty-one cases and calculated the deviations from average. These we find ± 3.8 per cent in the male subjects, ± 5.2 per cent in the female subjects and ± 5.7 per cent in the cardiac cases, with a total average of ± 4.9 per cent. Of equal significance is the close

*There is the possibility of course that the slight obstruction to inspiration which we introduce into our technic elevates the blood flow sufficiently to mask the tendency to low results. Huggett[13] has shown that cats show a markedly increased blood flow against an inspiration obstruction of 5 cm. of water. But this is an enormous obstruction for an animal of that size in no way comparable to an obstruction of 3 to 4 cm. of water in man. Blalock, Harrison and Wilson[14] have shown the same things on dogs but in their work too the degree of obstruction although unmeasured was so large as to cause marked work on the part of the animal to overcome it.

approach to constancy of the stroke index and of the a-v oxygen difference in our series of normal people. Thus, to recapitulate, in sixty observations the former showed a percentage average deviation of ±12, the latter ±11.

These data establish the method as clinically useful, on the ground that it is able to give constant and verifiable results, and point to the supposition that whatever errors are present to influence it away from "absolute" accuracy are uniform and constant, and probably clinically negligible.

SUMMARY AND CONCLUSIONS

The desirability of a clinical method for the blood flow determination, and the general principle upon which such methods are based, are outlined.

The Henderson and Haggard method, based upon the use of ethyliodide, is described and a critical analysis of its elements given. Two sources of error, in our experience, are defined: one concerned with the method of collecting alveolar air, the other with a return of a portion of the ethyliodide inhaled, in the venous blood. A slight modification in apparatus and technic is suggested in order to eliminate the former and evidence toward the effectiveness of which is presented. An estimate is made of the influence of the second error on the final results. Our technical experience is described.

Our results with this method in sixty determinations on normal male and female subjects, and twenty determinations on a miscellaneous group of decompensated cardiac patients, are tabulated. These are in accord with the results of the authors of the method and with the results obtained by other workers with other reliable methods. Our results agree in duplicate within a total percentage deviation from average of ± 5.

The average of our results is given in Table VII.

TABLE VII

OBSERVATIONS	BLOOD FLOW LITERS	STROKE VOLUME C.C.	STROKE INDEX	A–V OXYGEN DIFFERENCE
32 males	8.1	102	1.5	3.5
27 females	7.3	93	1.64	3.3
20 cardiacs	4.9	54	0.96	5.5

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INTERMITTENT INCOMPLETE BUNDLE-BRANCH BLOCK*

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IT IS occasionally found in electrocardiography that initial ventricular complexes which present marked changes in form and increased duration in all leads are subsequently replaced by complexes having normal characteristics. Many examples of permanent abnormalities of the QRS complex have been recorded and various descriptive names have been applied to them, such as intraventricular block, arborization block and incomplete bundle-branch block.

Considerable difference of opinion has prevailed regarding the nature of these abnormalities but experimental studies within the last few years have greatly clarified the problem. It is not necessary to review all the work bearing on the subject except to summarize the results of Wilson and Herrmann,[13, 14] Their work enabled them to conclude that delayed conduction of the cardiac impulse through one of the chief branches of the His bundle gave rise to ventricular complexes transitional in form between the normal complex and the complex of complete bundle-branch block. This concept is based on the form of the records obtained by the algebraic summation of the levocardiogram and the dextrocardiogram in varying time relations, the experimental combination of levocardiogram and dextrocardiogram and the form of the ventricular complexes obtained during the period of recovery that follows temporary bundle-branch block.

In the cases comprising the basis of this study there were electrocardiograms definitely conforming to those of incomplete bundle-branch block; that is, they were transitional in form between the complexes of complete bundle-branch block and normal complexes. The significance of these changes clinically, physiologically and anatomically are still problematical; therefore, we are presenting these cases in a further endeavor to correlate clinical and abnormal physiological findings.

Robinson[10, 11] discussed the transient abnormalities and reported one case to illustrate his views. He concluded that anatomical lesions were not necessary for the production of disturbances of intraventricular conduction but that the disturbance may result from "functional fatigue." He further advanced the hypothesis that the interference with conduction may be due to the presence of acid metabolites

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in the ventricular structures and that sclerosis of the coronary arteries and perhaps other lesions interfering with the nutrition of the heart are responsible.

Changes in the form of the ventricular complexes have been produced experimentally by vagal stimulation,[2, 4, 6] and have also been noted in clinical cases resulting from vagal influences.[7, 9, 12] Less striking alterations in the QRS complex have also been observed with changes in the position of the heart[1, 3, 5, 8] but are in no way comparable to the abnormalities under discussion.

REPORT OF CASES

CASE 1.—This patient, a nurse, aged sixty-five years, has been and is still actively engaged in hospital management. She sought medical advice on September 3, 1921, in order to protect herself as much as possible from the recurrence of a previous illness, which had begun nine months before. At that time the patient was forced to seek rest in bed because of general weakness and marked vertigo.

The family history was of no significance. The patient had had two definite attacks of acute rheumatic fever at the age of twenty-two and thirty-three years. Recovery from both these illnesses had been satisfactory. She also had noted slight dyspnea for several years on going upstairs. The first distinct cardiovascular break occurred nine months before our examination, the chief symptoms being general weakness, vertigo and nocturia. She remained in bed only a few days, but did not return to her hospital duties for a month.

The patient was up and about and quite comfortable and at work on the day of her examination; the pulse was regular in force and rhythm. There was slight peripheral sclerosis. The mucous membranes were of good color and there was no evidence of anemia. The systolic blood pressure was 170 mm. and the diastolic 80. The tonsils were moderately enlarged but showed no definite evidence of infection. There was no edema. On percussion the heart measured 3 cm. to the right and 11.5 cm. to the left of the midsternal line in the fifth intercostal space. The action was regular and there were no murmurs, although the sounds were perhaps slightly muffled. The edge of the liver was just palpable at the costal margin on deep inspiration. The ocular fundi showed mild arteriosclerotic changes.

From these physical findings a diagnosis was made of myocardial degeneration, compensated, and moderate generalized arteriosclerosis and essential hypertension. It was at this time that the first electrocardiographic examination was made and marked abnormality of the QRS complexes were found. The patient was advised to follow a diet with restricted protein and salt and reduce her weight to between 150 and 160 pounds. On January 26, 1922, her weight had been reduced to 155 pounds; the pulse was 70, regular in force and rhythm; the systolic blood pressure was 175 and the diastolic 85. The nonprotein nitrogen in the blood was 37 mg., creatinin 1.5 mg.; the result of urinalysis was essentially negative, there being no sugar and no albumin present.

On February 27 the patient was examined again. She had been very busy on the two previous days and early in the morning of this day she became dizzy and found that she could not raise her head from the pillow. The pulse was 72, quite regular, and the systolic blood pressure was 175 mm. and the diastolic 85. There was no edema, the lungs were clear and there was no evidence of any central cerebral lesion. She remained in bed for two or three days; she has had no such attack in the four years since.

Since her first examination in September, 1921, the patient has taken no medicine. She has adhered strictly to a low-protein, low-salt diet and has taken daily rest early in the afternoon and has guarded against stresses both physical and mental, although carrying on her regular work. On her last examination, January 15, 1926, the findings were essentially the same as when she was first examined four years previously. The systolic blood pressure was 160, the diastolic pressure 70 and the pulse rate 80.

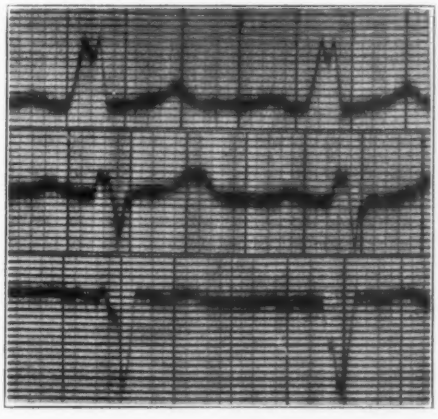

Fig. 1.—Case 1. September 3, 1921.

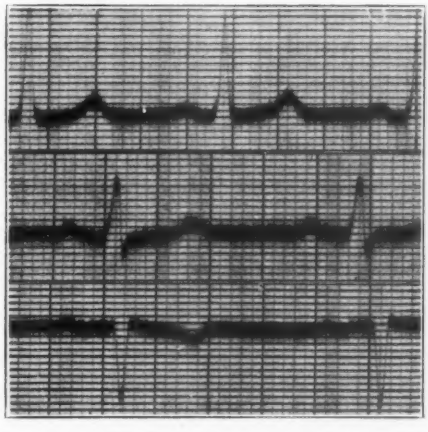

Fig. 2.—Case 1. January 23, 1922.

Discussion of Electrocardiograms.—The first record was obtained on September 3, 1921 (Fig. 1). Marked abnormality of the QRS complexes is evident in all leads. The interval is increased, being 0.14 second in Lead I, 0.12 second in Lead II and 0.12 second in Lead III. Distinct notching is present in all leads. The next record taken was on January 23, 1922 (Fig. 2), and shows normal ventricular complexes. The record obtained on July 19, 1922, is likewise normal (Fig. 3). January 5, 1924 (Fig 4), distinct abnormality of the QRS complexes

again occurred. The changes, however, are not so marked as those in the initial tracing. The subsequent records obtained on April 29, 1924, June 13, 1925, January 14, 1926, and October 13, 1926, constantly show abnormal complexes, and slight variations in contour of the aberrant deflections occur (Figs. 5, 6, 7, and 8).

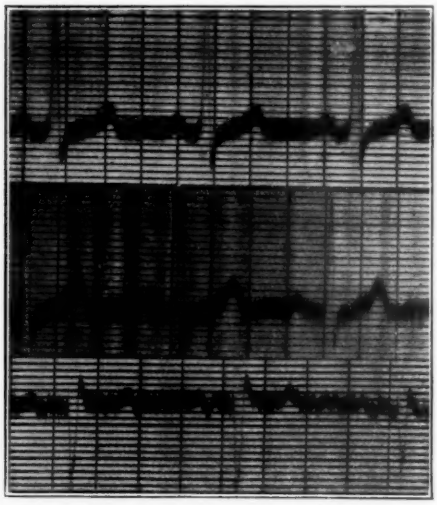

Fig. 3.—Case 1. July 19, 1922.

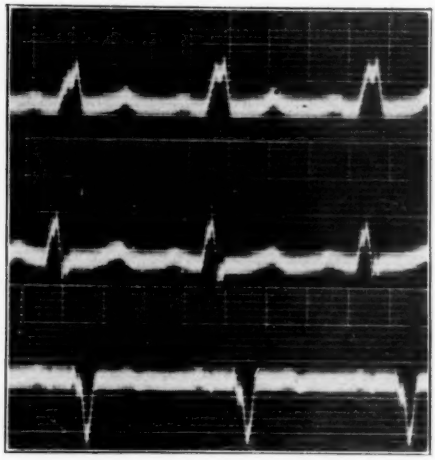

Fig. 4.—Case 1. January 5, 1924.

Comment.—This case is of unusual interest in view of the fact that the initial tracing showed marked abnormalities, limited to the QRS complexes in all leads, which subsequently disappeared for several months. The first tracing, however, was taken soon after the patient had recovered from an attack of mild cardiac decompensation.

The succeeding records, all obtained during the last three years,

essentially conform to the original record, yet during this period the patient has been in better health than at previous periods of our observation.

At no time while this patient was under observation during the last five years was any degree of clinical cardiac decompensation

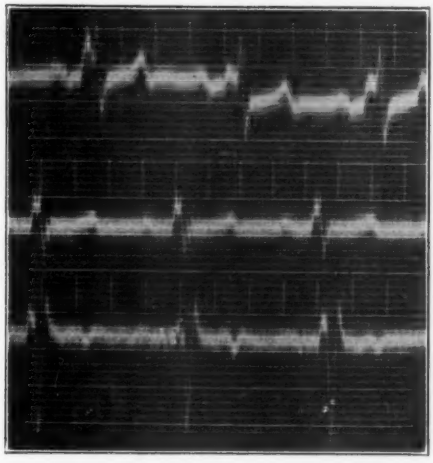

Fig. 5.—Case 1. April 29, 1924.

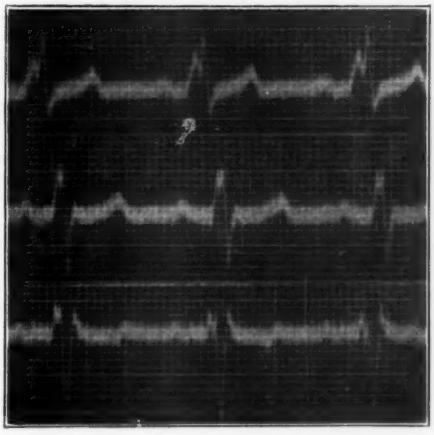

Fig. 6.—Case 1. June 13, 1925.

present. The patient is still living and very active in an administrative capacity.

These findings are obviously difficult to explain, yet it is possible that the abnormalities in the original electrocardiogram resulted from myocardial fatigue following the mild cardiac decompensation. On the other hand, the records obtained during the last three years were constantly abnormal, with little clinical evidence of cardiac fatigue. The constancy of the electrocardiographic phenomena dur-

ing the last three years suggests the possibility of anatomical myocardial changes having developed. These phenomena may be related to two severe attacks of rheumatic fever thirty-two and forty-three years ago.

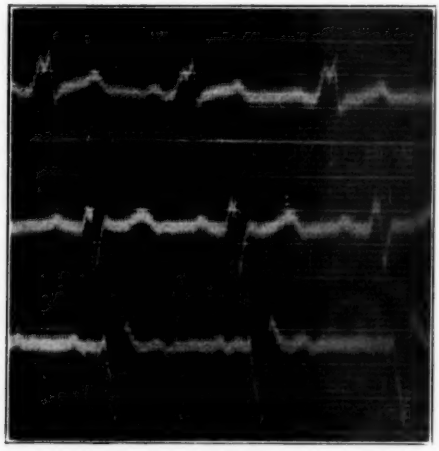

Fig. 7.—Case 1. January 14, 1926.

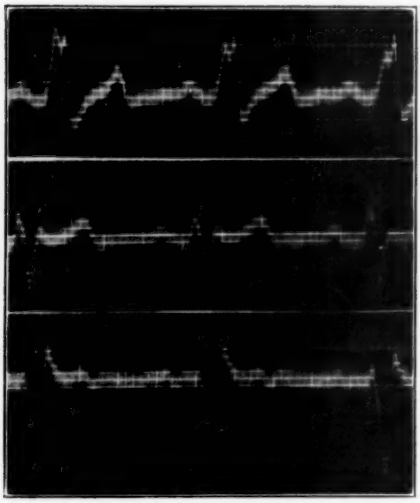

Fig. 8.—Case 1. October 13, 1926.

CASE 2.—A woman, aged sixty-six years, was admitted to the hospital during the early morning of Sept. 15, 1925, critically ill. The family history was unimportant. She had had an occasional attack of mild tonsillitis. She had been somewhat short of breath on exertion for the last two years but this had not been marked until the last two months. Walking up one flight of stairs recently caused marked breathlessness but she had managed to continue her duties as a dormitory matron. During the evening of admission to the hospital she quite suddenly became extremely short of breath and the breathing was very noisy.

On examination the patient appeared critically ill. Respiration was labored and rattling noises in the chest were audible. Marked peripheral cyanosis was present. She was covered with cold perspiration and the radial pulse was barely perceptible. The cardiac dulness extended 5.0 cm. to the right and 12.0 cm. to the left of the midsternal line. The tones were rapid and of poor quality. Many coarse, bubbling moist râles were audible over the entire chest. A slight degree of dependent edema was present. The systolic blood pressure was 144 and the diastolic 86. The pulse rate at this time was 98. Myocardial degeneration associated with coronary sclerosis and acute pulmonary edema was diagnosed.

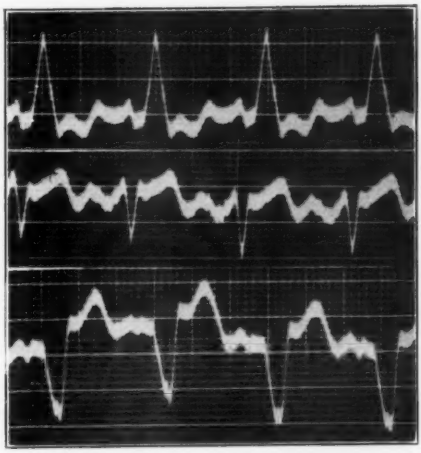

Fig. 9.—Case 2. September 15, 1925.

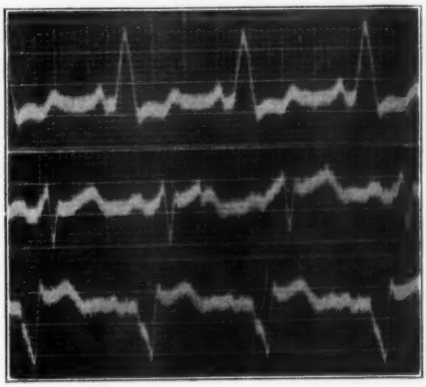

Fig. 10.—Case 2. September 18, 1925.

Atropine sulphate, 2 mg., was administered subcutaneously and was soon followed by the administration of nitroglycerin, 0.15 mg. Improvement in the patient's condition was remarkably rapid and by morning she appeared distinctly better. Tincture of digitalis was administered orally in dosage of 1.5 c.c. three times daily until a total of 12 c.c. was given. The electrocardiogram taken on the same morning showed the rate to be 103, and abnormal ventricular complexes of incomplete bundle-branch block. Repeated urinalysis showed only a faint trace of albumin and an occasional leucocyte in the centrifuged sediment. The blood urea was 24

mg. for each 100 c.c. of blood. The hemoglobin was 60 per cent (Dare) and the erythrocytes numbered 3,380,000. The blood Wassermann test was negative.

After uneventful and progressive improvement the patient was dismissed from the hospital October 15, 1925. Recent reports, fourteen months later, give information of satisfactory progress.

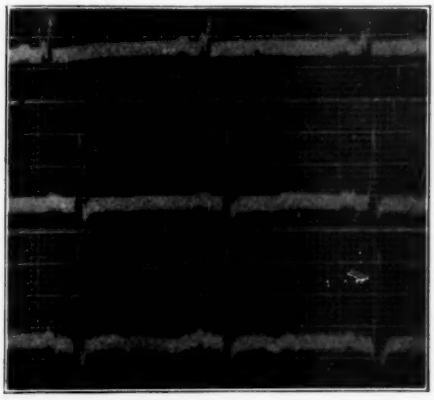

Fig. 11.—Case 2. September 22, 1925.

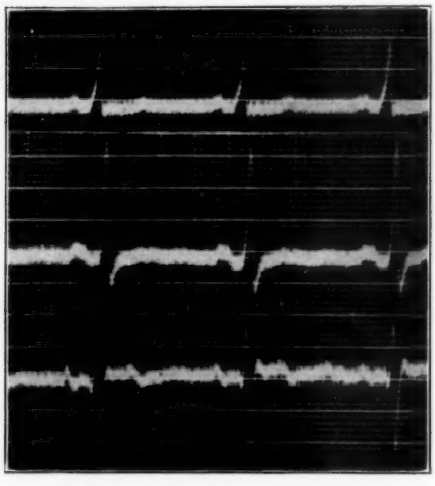

Fig. 12.—Case 2. October 14, 1925.

Discussion of Electrocardiograms.—The first electrocardiogram, taken September 15, 1925, shows the presence of abnormal ventricular complexes of incomplete bundle-branch block (Fig. 9). The QRS interval is 0.15 second in Lead I, 0.11 second in Lead II, and 0.13 second in Lead III. Distinct notching of the P-wave is present in Lead III while in Lead I the descending limb of the complex is slurred. The T-wave in Lead I is negative. The record obtained three days later is very similar (Fig. 10). A definite change occurred, however, in the form of the QRS complex in Lead III. The next record, taken four days later

(September 22), was practically normal (Fig. 11). Virtually all evidence of disturbance of conduction had disappeared. Slight notching of the QRS complex in Lead I was present. The last tracing (Fig. 12), obtained October 14, depicts further return to normal.

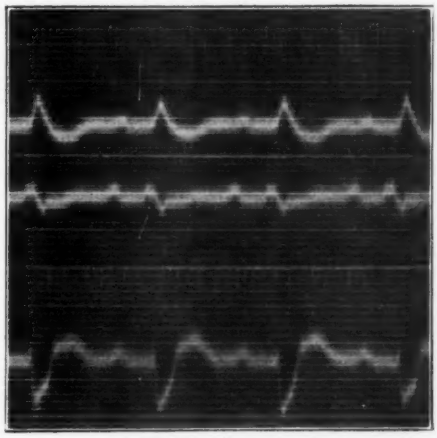

Fig. 13.—Case 3. November 4, 1924.

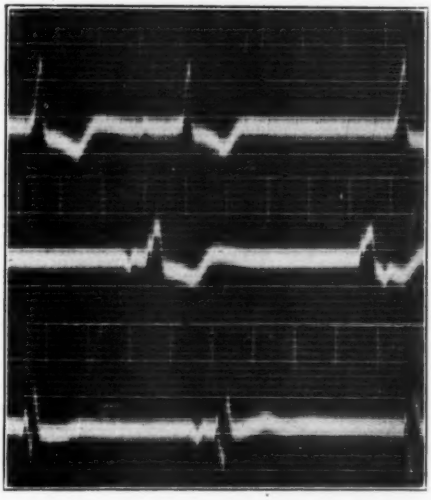

Fig. 14.—Case 3. November 5, 1924.

Comment.—It is not likely that the marked evidence of disturbed ventricular conduction in this case was the result of structural involvement of the conduction paths in view of the virtual return of the electrocardiograms to normal. It is probable, however, that profound physiological disturbances in conduction did occur as the result of the marked temporary myocardial failure. The electrocardiograms in this case parallel the clinical myocardial status.

CASE 3.—A man, aged forty-six years, was admitted to the hospital Nov. 4, 1924. The family history was unimportant. All illnesses were denied other than mild tonsillitis for which tonsillectomy had been performed a year previously. The patient began to be troubled with shortness of breath on effort three months previously, about the time that a distressing unproductive cough appeared. The shortness of breath increased in severity and one month later difficulty in breathing began to cause him very restless nights. The systolic blood pressure taken by his family physician at that time varied from 170 to 225. The patient knew nothing about the diastolic readings. There had been no edema.

The patient was very dyspneic, the facies was anxious and restlessness marked. The heart was enlarged, the area of dulness extending 4.0 cm. to the right and 13.0 cm. to the left of the midsternal line. Occasional premature contractions interrupted the rhythm. No murmurs were audible. The aortic second tone was markedly accentuated. A slight degree of peripheral arteriosclerosis was present.

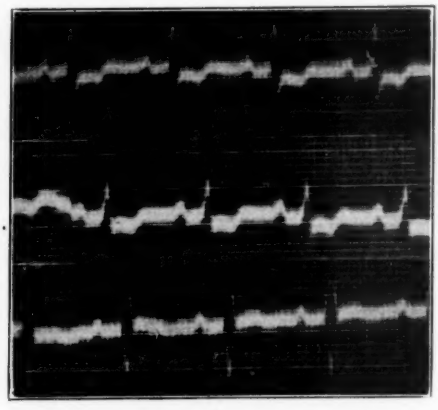

Fig. 15.—Case 3. November 11, 1924.

The systolic blood pressure varied from 184 to 194 and the diastolic from 140 to 146. The physical examination was otherwise unimportant.

Myocardial degeneration associated with hypertension was diagnosed. The electrocardiogram taken on the day of admission showed incomplete bundle-branch block. On repeated analysis of the urine the specific gravity varied from 1.018 to 1.022, a faint trace of albumin was constantly present and occasionally hyaline casts and a few leucocytes were found. The combined phenolsulphonephthalein test by the intravenous method revealed an excretion of 40 per cent of the dye in two hours. There were 43 mg. of urea in each 100 c.c. of blood. The creatinin reading was 1.7 mg. and the uric acid 3.7. The hemoglobin was 81 per cent (Dare), the erythrocytes numbered 5,230,000 and the leucocytes 12,400. The ocular fundi showed sclerotic changes of hypertension; small retinal hemorrhagic areas were present and small spots in the macular region.

The patient remained under observation eleven days and improved moderately. Death occurred from progressive myocardial failure eighteen months later.

Discussion of Electrocardiograms.—The first record (Fig. 13) showed marked abnormality of the QRS complexes. The interval was increased in all leads, measuring 0.12 second. Distinct notching occurred in all leads. The electrocardiogram obtained the following day revealed the presence of nodal and ventricular premature contractions

(Fig. 14). The QRS complexes were more normal in contour and duration. The record obtained six days later (Fig. 15) showed complexes that were practically normal.

Comment.—It is probable that the disturbance of conduction in this case, as in Case 2, was dependent on functional changes resulting from temporary fatigue of the myocardium.

SUMMARY

Three cases of intermittent incomplete bundle-branch block are presented with clinical notes and a discussion of the electrocardiograms. Certain features in these three cases warrant further emphasis. In all instances there was evidence of myocardial disease without endocardial valvular involvement. Cardiac enlargement was not marked in any case and slight dependent edema occurred in only one instance. Acute cardiac decompensation was present in two cases as evidenced by pulmonary edema, while in the other case no clinical decompensation occurred. These cases demonstrate that apparent profound disturbances in ventricular conduction may be evanescent, with or without cardiac decompensation. It is important to emphasize further that the electrocardiograph may be the first and only means of detecting serious myocardial changes, as is illustrated in Case 1.

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ATRIOVENTRICULAR NODAL RHYTHM*

Report of Two Cases Exhibiting Bigeminy

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Boston, Mass.

ATRIOVENTRICULAR rhythm, so-called "nodal rhythm," is an unusual condition. The rarity of the finding and the mechanism of its production, render it a more interesting study than its clinical significance would indicate, since it is usually of short duration and not serious. In a majority of cases it means depression of the sinoauricular node, thus releasing the automatic stimulus production in the atrioventricular node (of Tawara). Its experimental production has been well shown by Hering[1] and by Lewis[2] either by destruction of the sinoauricular node or by depression of it by cold or vagal stimulation. In human beings, the condition has been found by Wilson[3] and by White[4] directly after the administration of atropine. Its presence can be proved only by electrocardiograms in which the auricular complex (P-wave) must be inverted. This inverted P-wave generally follows the QRS wave; rarely it may precede it by a short interval.

Clinically, a number of cases have been recorded. The first report of a carefully studied case was made by White[5] in 1916. Richardson,[6] in a report of a case in 1922, considered that the literature contained 20 cases in all. More recently, cases have been added by Castellano and Tey,[7] Peters,[8] and Danielopolu and Proca[9] (2 cases).

The presence of coupled beats or bigeminy in cases of atrioventricular nodal rhythm is even rarer than the rhythm itself. In the case studied by White,[5] and referred to above, bigeminy occurred when the vs-as or R-P interval was markedly prolonged by digitalis or by vagal pressure. The coupling consisted of a sandwiching of an auricular contraction between two ventricular beats. When this occurred, the R-P interval was definitely longer than that found when there was merely atrioventricular rhythm. Thus, a delay in the passage of the excitatory process to the auricle allows the ventricle time to recover from its refractory period so that it may respond to the new stimulus. Another plausible explanation of the bigeminy is that abnormal auricular beats are excited mechanically by the idioventricular contractions, and these in turn are followed by ventricular responses. A second case was reported by White[10] in 1921, bigeminy occurring as before when the atrioventricular rhythm was slowest and the backward conduction of the impulse from the A-V node to the auricle the most retarded. Cases have been reported also by Gallavardin,[11] and by Bishop.[12] Recently

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Drury[13] has reported an unusual case of paroxysmal tachycardia of atrioventricular nodal origin, exhibiting at times reciprocal rhythm. When there was a sufficient delay in the auricular contraction, it in turn gave rise to a second ventricular response, causing bigeminy. Drury considers the mechanism of the rhythm as that given above, stating that for its occurrence it seems reasonable to consider that the impulse set free from the atrioventricular node reenters either in the auricular muscle or at some other supraventricular point and passes again to the ventricle, and that the junctional tissues are ready

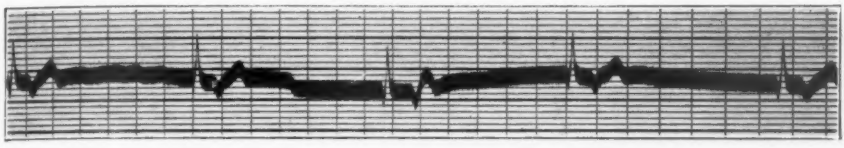

Fig. 1.—Case 1, (plate 10,048), L. L., Lead III. June 30, 1925. Atrioventricular nodal rhythm. Rate 40. R-P interval from 0.17 to 0.2 second. (In this and in all succeeding electrocardiograms, distances between ordinates represent 0.2 second, distance between abscissae 10-4 volts.

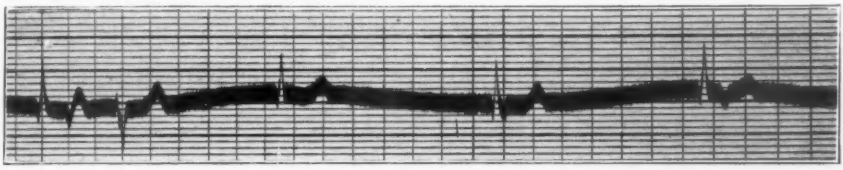

Fig. 2.—Case I, (plate 10,048A), L. L., Lead III. June 30, 1925. Bigeminy occurs once (R-P=0.2 second), with some aberration of the second ventricular complex. Following this no auricular activity is evident in the next complex. Nodal rhythm again occurs in the third complex with shortened R-P interval.

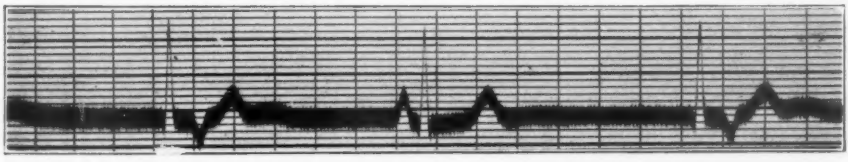

Fig. 3.—Case I, (plate 10,173), L. L., Lead II. Aug. 19, 1925. A-V nodal rhythm interrupted by normal or auricular premature beat with R-P interval of 0.12 second.

to conduct the reentrant impulse to the ventricle very shortly after they have conducted the impulse to the auricles.

The two cases herein reported present unusual variations and quite different clinical pictures. Case 1 showed merely cardiac enlargement clinically and was investigated because of bradycardia, found when she was examined for epigastric difficulties which were presumably due to two esophageal diverticula and to nervousness. Bigeminy was recorded only once (see Fig. 2) and that with an R-P interval of 0.2 second, which is as long as any R-P interval recorded on many of the tracings. Atrioventricular rhythm was the most constant finding, but

it is interesting to note that on one occasion normal rhythm (see Fig. 4) was present when the record was made in the recumbent position, while on the same day with records made when the patient was sitting up, atrioventricular rhythm returned. One record shows quite clearly

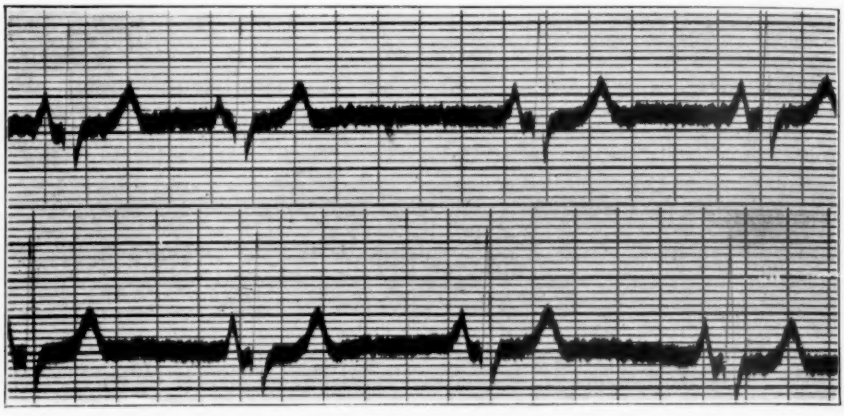

Fig. 4.—Case I, (plate 10,208), L. L., Lead II. Aug. 27, 1925. Normal rhythm. One auricular premature beat seen.

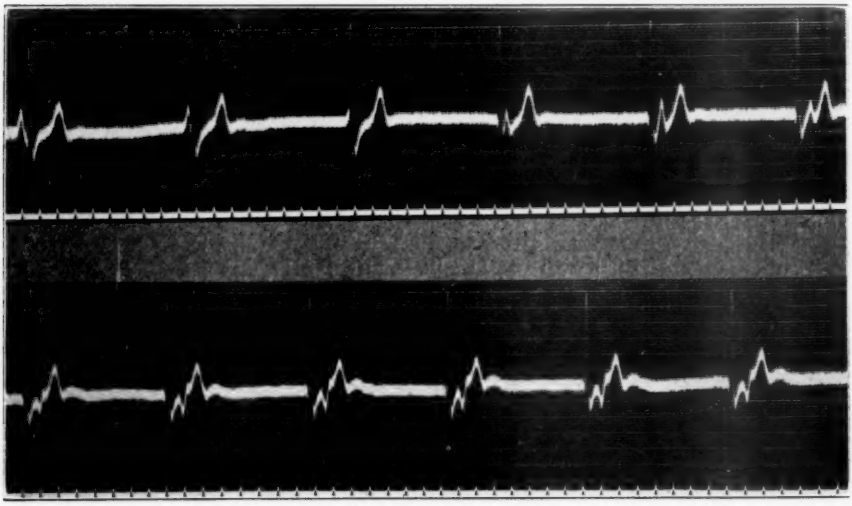

Fig. 5.—Case I. L. L., Lead II. Sept. 25, 1925. Continuous record. Independent rhythm (auriculoventricular dissociation) at the beginning with a heart rate of 35, atrioventricular nodal rhythm appearing with the seventh complex and the rate becoming 45. The auricular complexes of the independent rhythm occur at such long and increasing intervals that the ventricle escapes, and finally the atrioventricular node controls both auricles and ventricles. (Courtesy of the Peter Bent Brigham Hospital Staff.)

an independent rhythm (see Fig. 5) with definite upright P-waves arising apparently high in the auricle and gradually becoming lower, with the atrioventricular node finally assuming full control of the rhythm. On other occasions, there was a definite upright P-wave fol-

lowing the QRS complex (see Fig. 6). Certainly there must have been a marked auricular bradycardia and arrhythmia, with auricular systole falling often irregularly with respect to ventricular systole, and with the atrioventricular node controlling both the auricle and ventricle a large portion of the time. This indicates that depression of the sinoauricular node was responsible for the variations found.

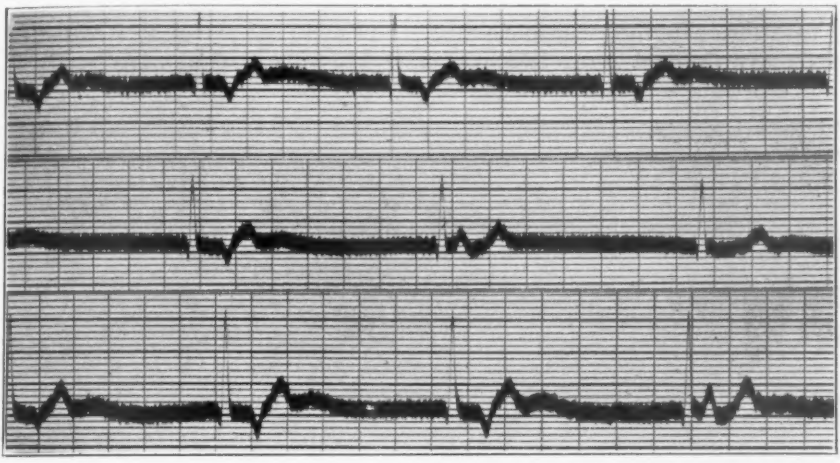

Fig. 6.—Case I, (plate 10,782A), L. L., Lead II. Jan. 28, 1926. Nodal rhythm persists, with some variation in the auricular waves, probably of similar origin to those in Fig. 5. The second P-wave of the second strip and the fourth P-wave of the third strip are not of atrioventricular nodal origin.

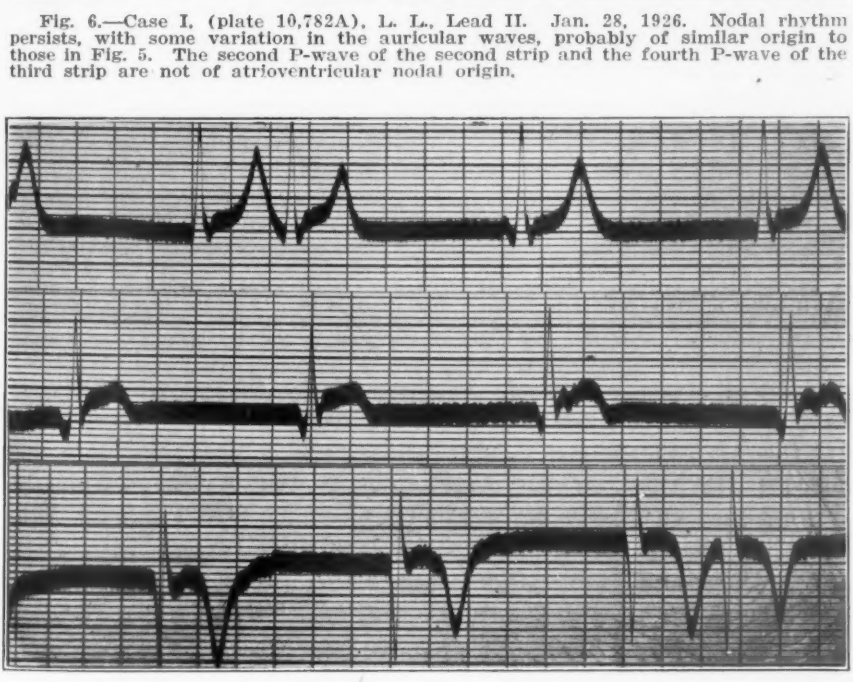

Fig. 7.—Case II, (plate 10,670), M. C., Jan. 4, 1926. Leads I, II, and III; no clear evidence of auricular activity except for possible inverted P-waves falling on the T-waves of the third and fourth complexes of Lead II. Ventricular rate 50, occasional bigeminy with a rate of 60 to 70. Abnormal T-waves.

There is probably a relationship between obstruction of certain coronary vessels and the function of the sinoauricular node and bundle of His and its branches. Géraudel,[14] in a recent communication, reports a patient with syphilitic aortitis, sixty-three years of age, who for more than a year showed what was most likely atrioventricular rhythm. Necropsy showed an obstruction where the artery supplying the sinoauricular node branched from the right coronary artery. Case 2 presents somewhat this possibility. Coronary occlusion with probable extensive cardiac infarction was present. The history and physical

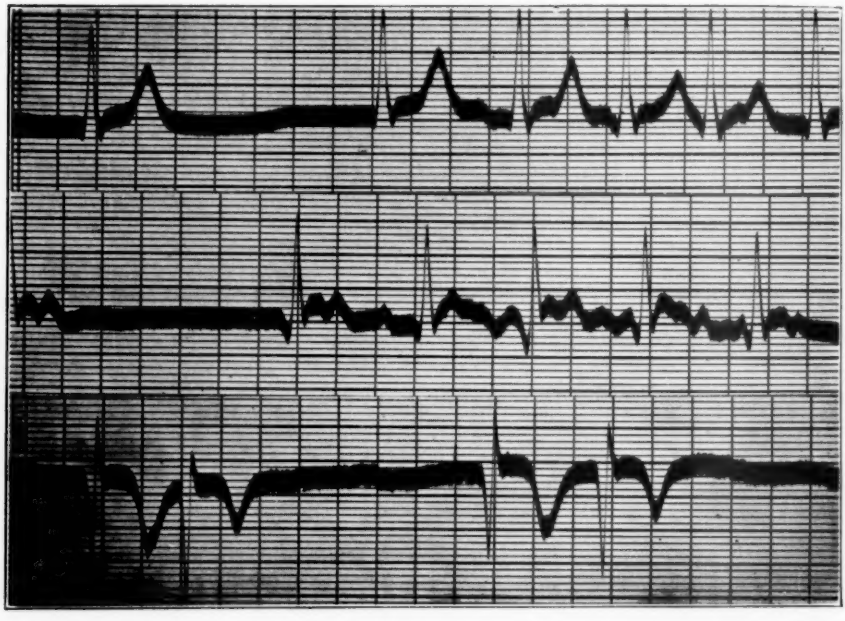

Fig. 8.—Case II, (plate 10,675), M. C., Jan. 5, 1926. Leads I, II, and III. Varying rhythm, at times atrioventricular nodal rhythm, rate 40, with inverted P-wave following the QRS complex; at times probable ectopic auricular tachycardia, with block or auricular arrythmia. Auricular rhythm rate is 100 and irregular. Abnormal T-waves continue.

findings were quite conclusive, as well as the electrocardiographic evidence and the patient's subsequent course. When first seen six days after the onset, an electrocardiogram showed no clear evidence of auricular activity, with an occasional bigeminy (see Fig. 7). This bigeminy persisted over a period of nine days (fifteen days after onset). Several days later there was evidence at times of atrioventricular rhythm, the inverted P-waves showing only in Lead II (see Fig. 8).

No record was obtained which showed the inverted auricular complex sandwiched between two ventricular systoles; this is due in all probability to the auricular complex having been merged with the very abnormal T-waves. It is natural to suppose that this is the

logical explanation of the very unusual coupling. Other abnormalities of the records are taken up under the history of the case.

CASES

CASE 1.—L. L., a Jewish widow of fifty years, was referred to the Cardiac Clinic, Out-Patient Department of the Massachusetts General Hospital, June 30, 1925, because of "bradycardia." The family history was negative except that her husband died with tuberculosis twenty years ago. There was a questionable history of rheumatic fever at the age of 30. For sixteen years she had been a patient in the Out-Patient Department. In 1910 she was treated for retroversion, lacerated cervix, and endocervicitis. From 1912 to 1915 she was treated for constipation and sacro iliac strain. In 1919 she had some pelvic operation elsewhere.

For many years she had had slight attacks of nausea, gas, and dull pain in the epigastrium, becoming worse in the late spring of 1925, for which condition she returned for treatment. The pain became nearly continuous and with sharp colic-like exacerbations coming directly after meals. This sharp pain radiated sometimes to the small of the back and to the right shoulder. The epigastrium had been tender, and at times a Seidlitz powder gave relief. Palpitation at times on exertion, and occasional precordial pain, never severe, were the only cardiac symptoms. At no time during the previous sixteen years had her pulse rate been recorded as below normal.

Examination showed the apex impulse of the heart and the left border of dulness in the fifth space, 8.5 cm. to left of the midsternal line, and 1 to 1.5 cm. beyond the midclavicular line. The rhythm was regular, with a rate of 42 per minute. Sounds were of good quality. At the apex and pulmonic area, a moderate systolic murmur was heard. There was no thrill, diastolic murmur, or edema. The radial arteries were slightly palpable. The brachial and temporal arteries were slightly tortuous and palpable, and the fundi showed moderate arteriosclerotic changes.

The blood pressure was 105 mm. mercury systolic, 65 diastolic. A teleroentgenogram showed some enlargement, particularly of the left ventricle, with a cardiothoracic ratio of 60.8 per cent. The Wassermann reaction was negative.

An electrocardiogram showed atrioventricular rhythm (Fig. 1) with a rate of 40, and an R-P interval varying between 0.17 and 0.2 second. Bigeminy occurred once (Fig. 2). Frequent records taken over a period of two months showed atrioventricular rhythm continuously, with variations from time to time in the length of the R-P interval. On Aug. 19, 1925, (Fig. 3) one questionably normal beat was seen with a P-R interval of 0.12 second. Aug. 27, 1925 nodal rhythm occurred as before when sitting up, but upon lying down normal rhythm (Fig. 4) with a rate of 52 was found. One auricular premature beat was recorded.

She entered the Peter Bent Brigham Hospital in September, 1925, for the same complaints, remaining there five weeks. Physical findings were essentially unchanged. X-ray examination revealed two small diverticula at about the mid-portion of the esophagus. The stomach and duodenum were frankly negative.

Frequent electrocardiographic records were made, of which a very interesting one is reproduced here (Fig. 5) showing an independent rhythm with a rate of 35, and the establishment of an atrioventricular rhythm toward the end of the record, with a rate of 45. Some records showed a very slow regular rhythm (sinoauricular bradycardia), at times with periods of complete asystole. Atropine sulphate by mouth (13 mg. in 5 days.), and later 2 mg. subcutaneously, did not affect the rhythm, or change the pacemaker. Adrenalin chloride (1:1000) subcutaneously, in 0.5 c.c. doses had no effect on two occasions. Barium chloride, 30 mg. four times daily, for 5 days, proved also to be ineffective.

February 6, 1926, she entered the Massachusetts General Hospital because of gastric symptoms, which had become more aggravated five weeks before. She was having a new symptom—intense substernal burning (called "heartburn"), with a point of maximum intensity about two inches above the ensiform cartilage, brought on by eating. With the burning there was occasionally a choking sensation and regurgitation. Electrocardiograms continued to show atrioventricular rhythm. X-ray films of the esophagus and stomach were essentially the same as those reported previously. After being placed on a light, bland diet, and at times having atropine sulphate or tincture of belladonna before meals, she began to improve, and had epigastric difficulty with burning sensation and regurgitation only at intervals. When seen last, September 7, 1926 her condition was the same as that of six months before. There was some decrease in her gastric symptoms, and she was little troubled by any heart symptoms. The last electrocardiogram was taken on the same date as the last visit, and continued to show atrioventricular rhythm, at times exhibiting auricular arrhythmia, like that seen in Fig. 6. Atrioventricular rhythm had been present almost constantly for at least fourteen months.

Case 2.—M. C. Male, aged 57 years, Jewish cobbler, entered the Massachusetts General Hospital on January 2, 1926, because of severe low substernal pain. The family history was negative. For the past ten years he had been seen at intervals in the Out-Patient Department, varying diagnoses having been made of psychoneurosis, laryngitis, and frontal sinusitis. In December, 1924, he was found to have a blood pressure of 230 mm. mercury systolic, 100 diastolic. Shortness of breath on exertion and tiring easily, were his chief complaints. He was thought to have hypertensive heart disease at that time.

Six days prior to his hospital entry the present illness began, though he had suffered with dyspnea on slight exertion for six or eight years. In the early morning he had felt nauseated and finally vomited, remaining in bed. That afternoon while trying to get out of bed he was suddenly seized with a terrific, sharp pain in his low substernal region, which apparently did not radiate. At the same time he was forced to "puff for air" and felt as though he were going to die. There were large gaseous eructations, and his face and hands became cold and blue, associated with a feeling of weakness and being very faint. A physician gave him some tablets, probably nitroglycerine, to dissolve under his tongue every half hour, but these gave no relief. Exertion in bed increased the pain. Twenty-four hours later he was again given tablets by mouth which gave him some relief. Four days later, upon attempting to go to his store, the pain became much worse, and while slowly walking home, it became so intense that he had to be taken home in a car. From that time until admission he had remained in bed, propped high with pillows, very dyspneic, and having continuous substernal pain.

Physical examination revealed an obese, dyspneic, elderly man with cyanosis of the lips and hands, sitting up in bed, apparently in severe pain. There were moist râles at the bases of both lungs, with dulness and diminished breath sounds at the right base. The apex impulse of the heart was not seen and could not be felt. Percussion was unsatisfactory because of the thick chest wall. The sounds were faint, distant and of poor quality, with a rate of 40, and some irregularity. The liver edge was questionably palpable. No edema of the extremities was present. The blood pressure was 120 mm. systolic, 80 diastolic. The temperature was 102.4° and the white blood cells were 18,200. The Wassermann reaction was negative. An electrocardiogram showed what was thought to be an idioventricular rhythm with a rate of 50 (Fig. 7). There was occasional bigeminy, increasing the rate to 60 or 70, and no clear evidence of auricular mechanism was found although two inverted P-waves suggesting atrioventricular nodal rhythm were considered possible.

Aberrant ventricular complexes were present in all three leads, with a very high T_1; abnormal T_2, and deeply inverted T_3. There was a great deal of doubt as to what mechanism was present, and the following were considered the possibilities, in the order of their probability; 1. Atrioventricular nodal rhythm with obscure P-waves; 2. Auricular bradycardia and arrhythmia; 3. Auricular standstill, and 4. Auricular fibrillation.

A diagnosis of coronary thrombosis was made, and large doses of morphine sulphate given to relieve the pain. No digitalis was prescribed. Opiates relieved the pain for the most part, but for nearly a week it remained fairly intense.

Frequent electrocardiographic tracings were taken. On Jan. 4, 1926, no change was found from the record of two days before. Jan. 5, 1926, varying rhythm was present, at times atrioventricular nodal rhythm, with definite inverted P-waves following the QRS complex. Again at times there was a tachycardia present,

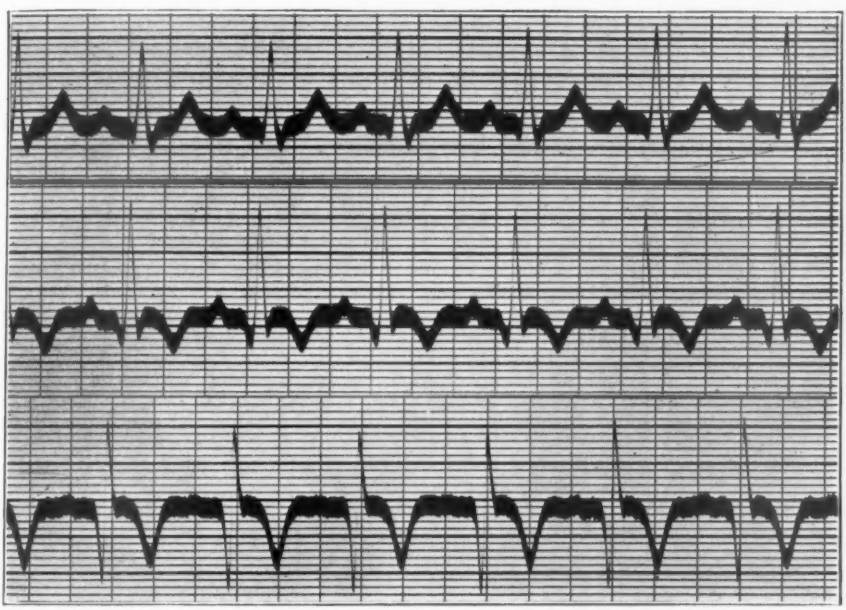

Fig. 9.—Case II, (plate 10,804), M. C., Feb. 4, 1926. Leads I, II, and III. Normal rhythm. Rate 95. Inverted T-waves in Leads II and III. QRS II is wide.

either sinoauricular or more likely of ectopic auricular origin. There were some beats with a slow rate, 40, probably idioventricular rhythm. The auricular rate at times was 100 and irregular. Abnormal T-waves were still present. Bigeminy was found in one lead, and was thought to be nodal bigeminy (see Fig. 8). On Jan. 6, 1926 there was regular rhythm, questionably nodal rhythm, with obscure P-waves and a rate of 45. For the next several days, the only change noted was in the T-wave, which seemed to be gradually becoming reduced in amplitude. On Jan. 11, 1926, normal rhythm was present and the T-wave in Lead II was inverted for the first time, associated with an upright T_1 and inverted T_3. There was also present a wide Q in Lead II, and left axis deviation with an index + 34, and an angle of minus 30°. T_1 had gradually become reduced in amplitude, allowing the still deeply inverted T_3 to have an effect on the T_2, and hence to cause its increased inversion. Ten days after admission, he felt much better, had little pain and was

anxious to go home. An electrocardiographic record taken Feb. 4, 1926, just prior to discharge, showed no change from the record of nearly a month before. The rhythm was normal, and an inverted T-wave occurred in Leads II and III, with a wide Q in Lead II. (Fig. 9.)

For one month after leaving the hospital he remained in bed, and was gradually allowed to return to work a few hours a day, according to his symptoms. Several electrocardiographic tracings taken since this time have showed no essential change. On the visit made to the Out-Patient Department Aug. 26, 1926 he was in fairly good condition, with substernal pain occasionally on exertion; he was able to work half the day. Two and one-half weeks after a second attack of coronary thrombosis at the end of October, 1926, he died suddenly at home. There was no postmortem examination.

SUMMARY

Atrioventricular rhythm in itself is a relatively rare condition, and bigeminy occurring during this rhythm is still more infrequently found. Two cases exhibiting this finding are presented, with electrocardiographic studies and discussion of other interesting features.

Thanks are due to the Medical Staff of the Peter Bent Brigham Hospital, particularly Dr. S. A. Levine, for notes and electrocardiogram of Case No. 1.

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HEART DISEASE FROM THE POINT OF VIEW OF THE PUBLIC HEALTH*

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THE subject of heart disease has become a matter of great public interest since it was pointed out a few years ago that the death rate on this account seemed to be rising. It soon became established that a rise has actually taken place. The experience with tuberculosis and with other infectious diseases suggested the idea that assiduous attention to heart disease like that which had been devoted to these other ailments might yield similar reductions in morbidity and mortality. Associations for the prevention and relief of heart disease were accordingly formed. It was only later, in more recent years, that certain facts began to be subjected to more searching analysis in order to learn, especially from the point of view of prevention and relief, what actually is the situation in respect to this group of diseases. For it required no great amount of reflection to appreciate the fact that, unlike tuberculosis or any other disease of bacterial origin, heart disease, or what went by this name, was composed not of a single entity but of diseases etiologically as distinct as the acute rheumatic affections, syphilis and arterial degeneration. At first it was not clear, and indeed in a general way it is not clear now, either in this or in point of fact in other connections, that arterial decay and degeneration of the heart might not be not diseases but the expression of the senescent process. To give expression to the underlying facts we shall in the end, perhaps, be obliged to make a distinction between the decrepitude of old age, a normal and natural growth process, and diseases in old age. That this distinction has importance in the problem I am to discuss, considerations later to be urged may make apparent.

When the increase in diseases in connection with the circulation became evident it was natural to compare the curve of death rates as the result of chronic diseases with that of the total death rate curve.

Fig. 1 illustrates the result of this comparison in New York City for the years 1868-1921.[1] At the beginning of this period the ratio of deaths from chronic diseases to the total death rate was about as 1 is to 15. At the end of this period the ratio was about as 1 is to 2. It appears, therefore, that the chronic diseases have taken on a quite new importance. The reason for this is seen in part in studying

*From the Hospital of the Rockefeller Institute for Medical Research, New York. Delivered as a De Lamar Lecture at the School of Hygiene and Public Health, Johns Hopkins University, Baltimore, November 15, 1926.

during the same period of time the changes in death rate which have taken place in certain acute diseases, such as diphtheria, scarlet fever, whooping cough and typhoid fever as exemplified in New York City. (See Fig. 2.)

After 1882 the curves of all of these diseases began to fall and after 1894, when antitoxin against diphtheria was first used, to fall significantly. It is perhaps worth pointing out that the fall occurred even in those diseases against which there was no specific antidote.

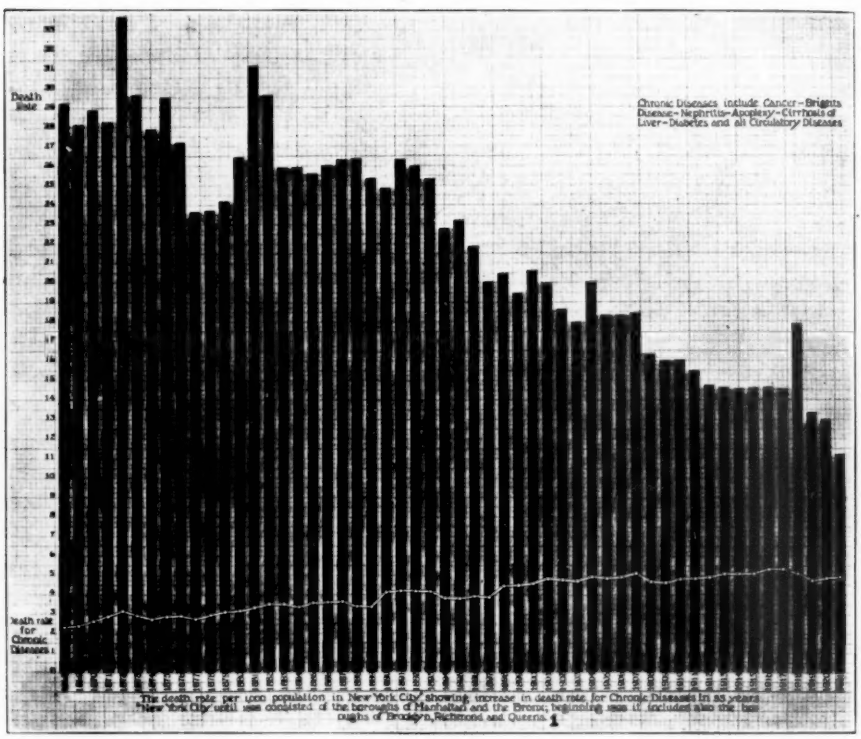

Fig. 1.

That the fall in infectious diseases might influence the death rate movement in heart disease also requires consideration. (See Fig. 3.)*

That the figures before 1900 are unreliable, due to the many phases of faulty technic employed in collecting them, is notorious. For this reason they probably fail to exhibit the course of events and can do no more than represent an approach to the facts. This is unfortunate in view of the important inferences which could otherwise have been drawn. It is, however, important to call attention to the inferences which are implied in considering them.

*I am much indebted to Miss Alice Whittemore for accumulating the data on which this curve is based and for arranging these curves as well as those in Fig. 4.

Before 1896, the curve *C* of chronic circulatory diseases exclusive of acute circulatory disease rose gradually. For this rise I have as yet no explanation to offer. In the moving average of this curve in the year 1896 there is a sharp inflection, the section afterward showing an abrupt rise. The foot point of the rise is referable probably to the year 1898 in curve *C*. The high point of the curve *A B D* of infectious diseases is found seventeen years earlier, in the year 1881. I entertain the belief, as do many others, that the fall in infectious dis-

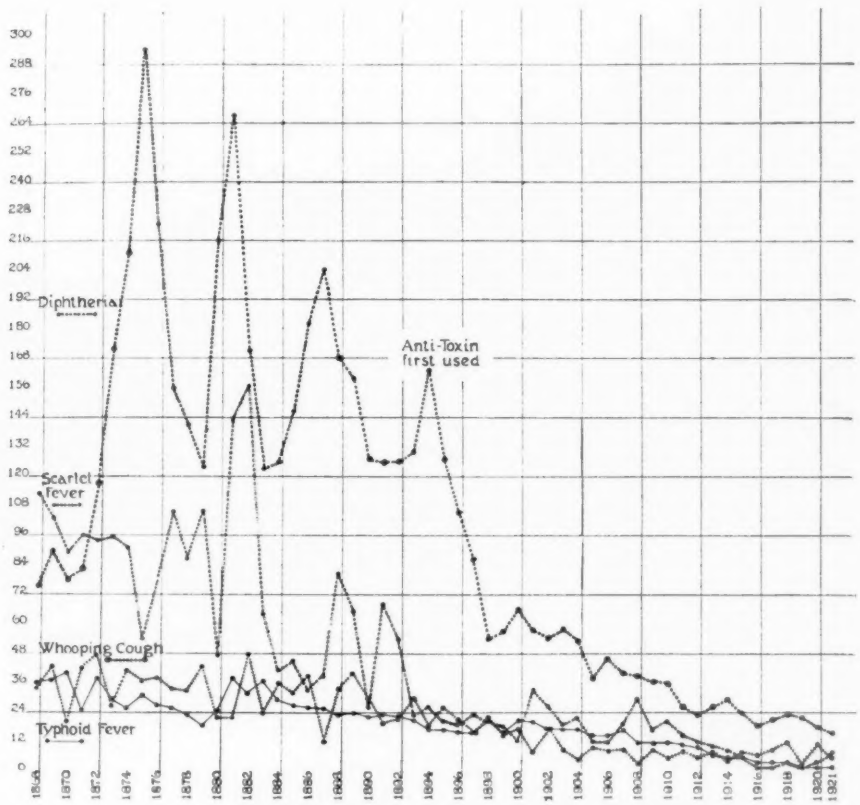

Chart showing decrease in death rate per 100,000 population in New York City for Typhoid-Diphtheria-Whooping Cough and Scarlet Fever during the past 53 years

Fig. 2.

eases is intimately related with the rise in the cardiac death rate. But I hesitate to state that precisely seventeen years are required after the beginning of the fall of the curve of infectious diseases before a beginning of the rise of the circulatory curve may take place. I should, in any case just now, be at a loss to suggest a proper explanation for the occurrence of exactly this interval. Perhaps the collection of the reports on which these curves are based was open to too many errors

MORTALITY RATES PER 100,000 OF VARIOUS DISEASES IN FIRST TEN REGISTRATION STATES PLUS DISTRICT OF COLUMBIA. 1868-1923.

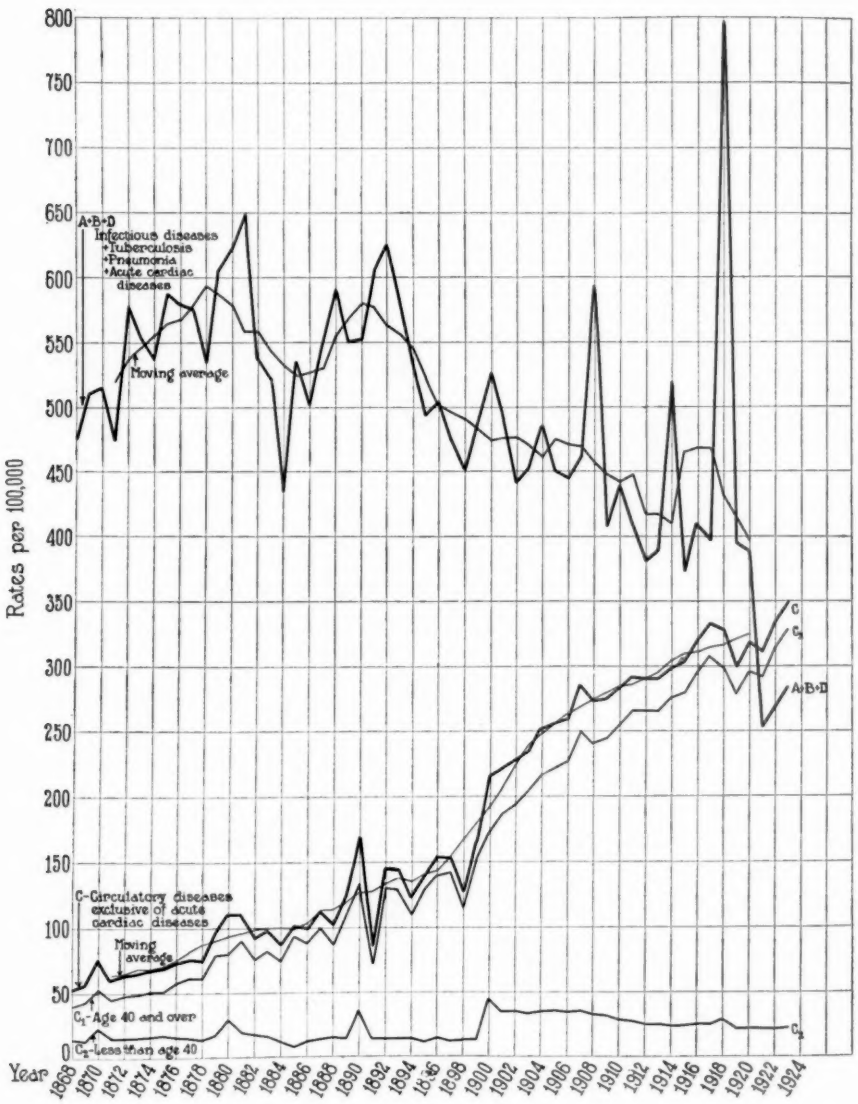

Fig. 3.

Diseases grouped as follows:

A—(Infectious diseases)
Typhoid fever
Measles
Scarlet fever
Whooping cough
Diphtheria
Influenza
Mumps
Dysentery
Acute poliomyelitis
Meningococcal meningitis
Malaria
Cholera nostras

B—
Tuberculosis
Pneumonia
Bronchopneumonia

C—(Circulatory diseases exclusive of acute cardiac diseases)
Apoplexy
Angina pectoris
Other diseases of the heart (including endocarditis)
Diseases of the arteries
Other diseases of the circulatory system

D—(Acute cardiac diseases)
Pericarditis
Acute endocarditis and myocarditis

States included: Connecticut, Indiana, Maine, Massachusetts, Michigan, New Hampshire, New Jersey, New York, Rhode Island, Vermont, and District of Columbia.

of diagnosis or of recording to make valuable the inferences which the curves so clearly suggest. But it seems, taking the general movement of the two curves into consideration, that being saved from infectious diseases preserves the population for exposure to death from more chronic or, from the viewpoint of the aging process, more natural death. It would be rash however to assert that the second process begins seventeen years after the decline of the first.

Infectious diseases may be divided into two groups, in one of which are included tuberculosis and pneumonia and in the other, the other acute infectious diseases as is shown in Fig. 4. It appears, as a result

MORTALITY RATES PER 100,000 OF VARIOUS DISEASES IN FIRST TEN REGISTRATION STATES PLUS DISTRICT OF COLUMBIA. 1868-1923.

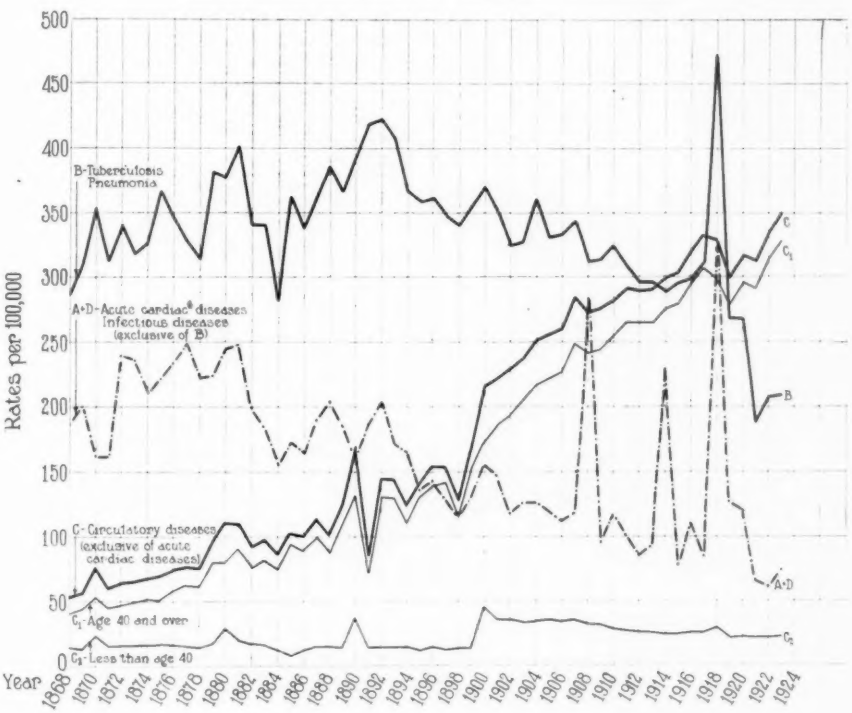

Fig. 4.

Diseases grouped as follows:

A—(Infectious diseases)
Typhoid fever
Measles
Scarlet fever
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Dysentery
Acute poliomyelitis
Meningococcal meningitis
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B—
Tuberculosis
Pneumonia
Bronchopneumonia

C—(Circulatory diseases exclusive of acute cardiac diseases)
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Pericarditis
Acute endocarditis and myocarditis

States included: Connecticut, Indiana, Maine, Massachusetts, Michigan, New Hampshire, New Jersey, New York, Rhode Island, Vermont, and District of Columbia.

of making this arbitrary division, that if the acute infectious diseases had a share in bringing about the rise in the death rate of circulatory diseases, little influence may be attributed to pneumonia and tuberculosis, for the fall in the curve of these two diseases does not occur until later. It must in consequence be the other infectious diseases, represented in curve *A D*, which may be associated with the change.

These relations tell the story of the changes which took place in heart disease when compared with mortality in general and with certain acute infectious diseases, but it does not suggest its relative importance in connection with other major causes of death such as pulmonary tuberculosis, pneumonia and cancer.

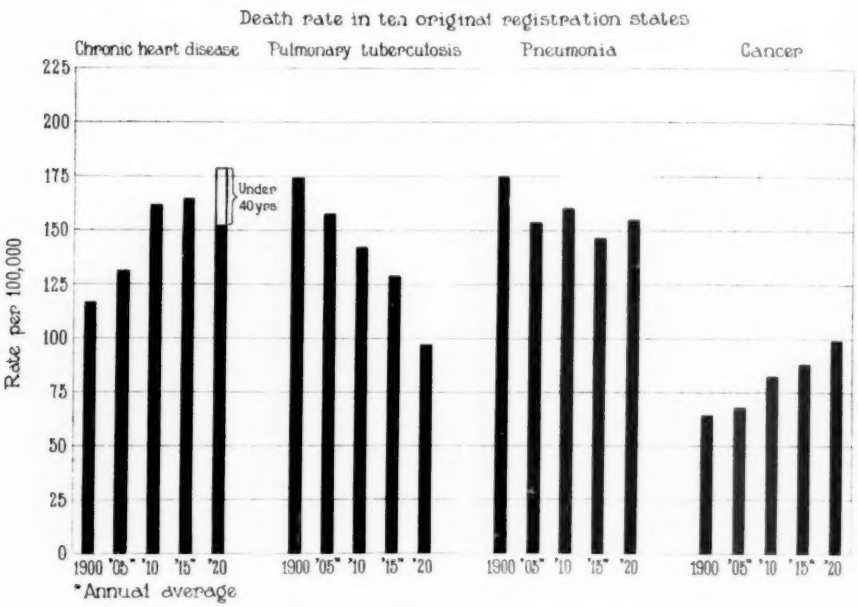

Fig. 5.

How heart disease increased during the twenty-year period from 1900 to 1920, how the rate from pulmonary tuberculosis fell, how the rate from pneumonia has not reached that of heart disease since 1910 and how cancer is mounting but is even now relatively speaking a small problem numerically compared to heart disease is illustrated in Fig. 5. One detail is indicated here to which I wish especially to direct your attention. You will find it in the heart disease group in the 1920 column. The point I refer to is that, of the total death rate, the proportion which occurs under the age of forty is relatively small, indeed only one-sixth.

That the high rates from heart disease which are encountered in the United States and in large cities like New York are not characteristic

of this country, a comparison with other nations and with other cities makes clear. (See Fig. 6.)* In studying data such as those I am about to present, I must repeat the warning that they do no more than suggest what sort of information should be available, that they are indeed removed from the possibility of being accurately representative. This state of affairs is, of course, deplorable; one of my purposes, however, consists in indicating how inadequate the data are

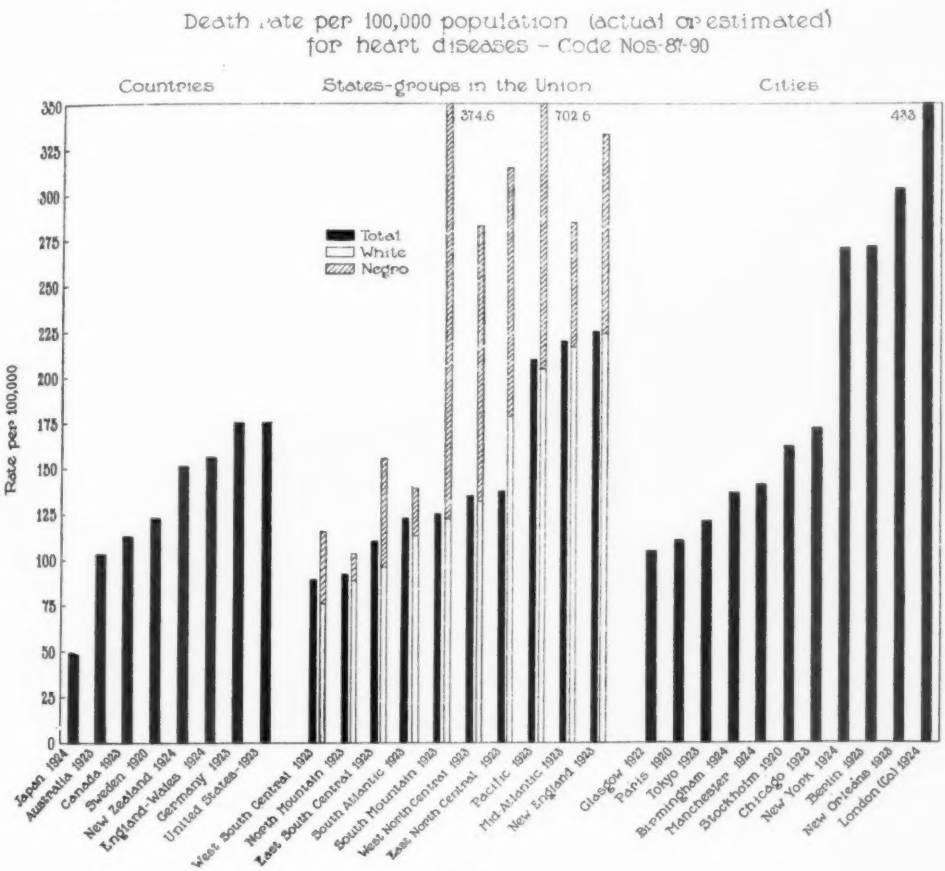

Fig. 6.

and how important it is to suggest the directions in which improvement is desirable.

For the year 1923 the rate in Germany, 175 per 100,000, is the same as that in the United States. England and Wales and New Zealand are not far removed. If there were time it would be interesting to discuss the low rate in Japan. A consideration of the rates in the cities shows that although the New York rate is not far removed from

*I am indebted to Miss Claire Lingg of the Heart Committee of the New York Tuberculosis and Health Association for the data in this figure.

the median, and that Berlin, New Orleans, and London all show higher rates, its rate as well as that of these cities is greater than that of the United States Registration Area. The same observation applies to Berlin and London in respect to Germany and to England and Wales.

The question has often been raised whether latitude and longitude and climate influence the incidence and, in consequence, the death rate from cardiac diseases. In the United States, if a report is made according to the geographical division of the states, it appears that the Southern and Mountain States at the left of the middle group of columns, present distinctly lower rates than the Pacific, New England or the Middle Atlantic States as is shown in this illustration. Similar relations are obtained by comparing death rates from *rheumatic fever* rather than from heart disease in various countries. (See Table I.[2]) I must point out, however, that to quote death rates from rheumatic disease is very different from quoting death rates for heart disease for although, especially in the younger age groups, rheumatic fever is a common cause of heart disease, there is no fixed ratio between its occurrence and the number of individuals who develop heart disease.

It appears, for example, that the rate from rheumatic fever is especially low in the Straits Settlements, Honduras, and Jamaica but high in New South Wales, England and Wales, and Ceylon. In the Straits Settlements, Honduras, and Ceylon the rates are calculated on the basis of the whole population, whereas in Jamaica on that of Europeans only. In the British colonies the low rates in the tropics may of course in part be due to the British custom of sending children to school in England at just those years at which the incidence of rheumatic fever is highest. In connection with locality there seems good reason for believing that rheumatic fever is more prevalent in Boston (295 cases or 1.85 per cent of admissions to the Peter Bent Brigham Hospital) than in Oklahoma City (14 cases or 0.1 per cent of admissions to the State University and to St. Anthony's Hospitals[3]). In the same cities and hospitals mitral stenosis, a disease which is postmortem easily distinguishable and is regarded as a peculiarly characteristic rheumatic disease, occurred in 4.69 per cent of 1362 autopsies and in none of 383 autopsies respectively. A similar observation has been published on the difference between the University of Virginia Hospital and the Massachusetts General; in the former chorea and rheumatic fever represented 0.7 per cent of admissions, the latter 1.3 per cent.[4] In comparison, however, with all these figures it is striking that in Northern countries, such as Denmark, Italy, Prussia, and Norway the rates are almost as low as in the tropics. And in point of fact as great a range in rates is found in the northern cities in Europe and in the United States. The influence of latitude in any case is not clear and requires further and more detailed studies. In

TABLE I

RHEUMATIC FEVER IN VARIOUS COUNTRIES AND CITIES*

Death Rate per 1000 Deaths

STATION	YEAR	RANGE OF YEARS	RATE PER 1000 DEATHS	AVERAGE RATE	RANGE				
					RATE		YEAR		
					MAX.	MIN.	MAX.	MIN.	
1. Str. Settlements	1904		0.27						Whole population. All nationalities
2. Honduras	1903		1.01						Whole population
3. Jamaica	1903		1.64						Europeans only
4. N. S. Wales	1903		4.48						
5. England and Wales	1903		4.62						
6. Ceylon	1903		6.78						Whole population. All forms of rheumatism
1. Denmark		1894–1903		1.10	1.42	0.71	1897	1902	
2. Italy		1894–1902		1.21	1.38	1.06	1899	1894	
3. Prussia		1894–1902		2.37	2.57	2.22	1902	1898	
4. Norway		1894–1903		2.86	3.11	1.98	1902	1898	
1. Paris		1901–1903		1.91	2.14	1.75	1903	1902	
2. Christiania		1894–1904		2.35	3.55	1.29	1903	1904	
3. Berlin		1894–1904		2.38	3.53	1.42	1900	1894	
4. Copenhagen		1894–1904		3.23	5.02	0.92	1897	1902	
5. New York City and Brooklyn		1899–1904		3.48					

*From W. S. Church. Rheumatic Fever. Allbutt & Rolleston's "System of Medicine," ii, 594-645.[2]

this connection the influence of season on deaths has also been explored. In London, for example, the seasonal influence on heart disease has been studied over a period of many years. (See Fig. 7.) It appears in the second curve quite clearly that in the winter months the number of deaths uniformly rises synchronously with those of the respiratory infections, but curiously enough not with those of influenza.

In New York a similar record has been kept since 1914. (See Fig. 8.) The curves from the point of view now being considered resemble those of London but show a closer relation between deaths

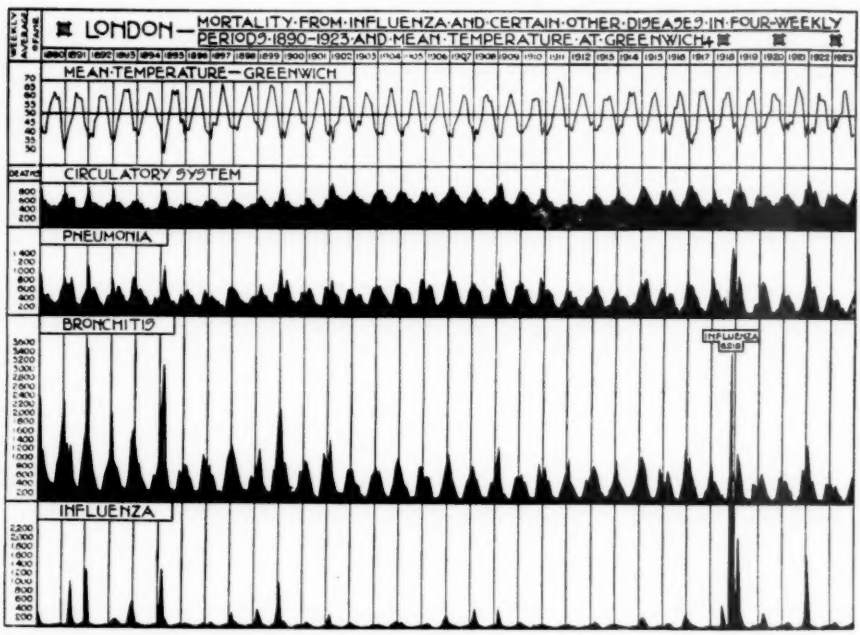

Fig. 7.

*See reference No. 5.

from heart disease and from influenza. There are added here curves for tuberculosis and for cancer.

So far, I have dwelt on the place of heart and circulatory diseases in their relation to mortality. The matter is difficult enough to analyze from this angle. But it should be analyzed also from the point of view of morbidity. Here the difficulties, however, increase. I need scarcely point out that I refer to such matters as inaccuracy in diagnosis and incomplete and erroneous reporting, not to mention differences in definition and in classification which are used in various localities. On the whole, though, these diseases are so characteristic that they do not easily escape detection, and the custom which has been introduced of reporting in accordance with the International

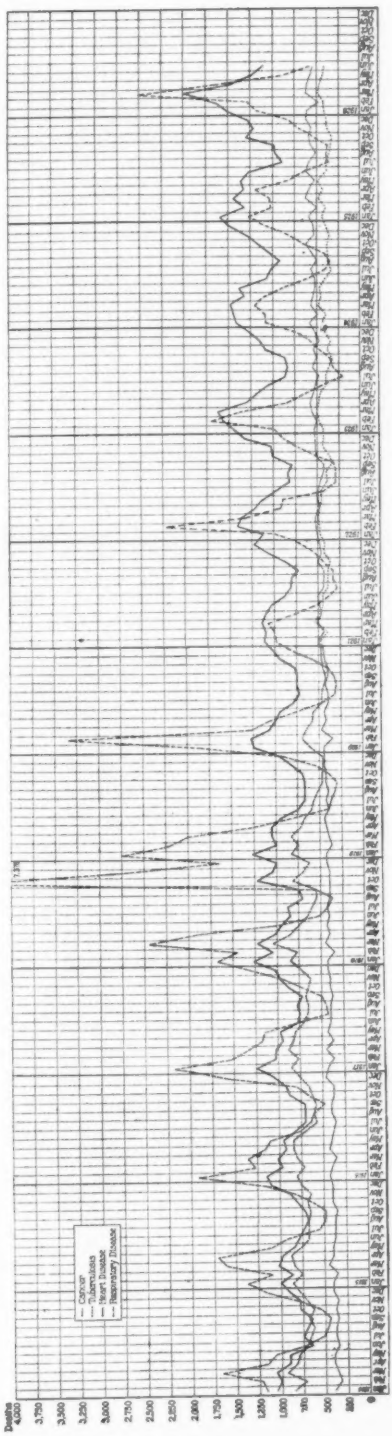
Mortality in New York City from chronic heart disease, all respiratory diseases, cancer and pulmonary tuberculosis.
Deaths
4,000
3,750
3,500
3,250
3,000
2,750
2,500
2,250
2,000
1,750
1,500
1,250
1,000
750
500
250
0
Cancer
Tuberculosis
Heart Disease
Respiratory Diseases

Fig. 8.

List of Causes of Death has reduced the trouble and has made it possible to place some reliance upon the published figures. From a study of certain morbidity statistics the great importance of the heart diseases also emerges. Data may be drawn from sources so varied as the draft in the United States and in England during the Great War; from statistics such as those of life insurance companies and of the British Insurance Act; from occupations, such as that of newsboys; from the incidence of heart disease in schools both here and abroad; as well as from hospital statistics. (See Table II.) Clearly these are in each case samples only of the population, which need not necessarily be characteristic, as Greenwood and Thompson[6] point out in the case of hospitals.

For the moment, however, data such as these represent the most reliable sources of information. We begin to emerge from a time, not long back, when hospital statistics were the staple in this field. In the United States draft during 1918, of 2,510,791 men, 85,143 or 26.26 per 1,000 were found to have valvular disease of the heart. Among Scottish troops during 1916-17, "whilst still fairly representative," the rate was similar, being 24 per 1,000. Among 1,000 recruits examined for the United States army at New York City in 1926[8] the rate was 15 per 1,000. Data are quoted by Miller to show that there is a difference in incidence between country and city. In the Channel Islands among recruits in 1901-1910, the rate was 1.0 per 1,000 as against 32.4 per 1,000 in the East Riding of Yorkshire. And in Wales during the Great War, among youths eighteen years old, the rate in Carmarthen was 2.0 and in Cardiff 22.0 per 1,000. In the United States on the other hand such striking differences are not discernible. There is no difference between agriculturists and manufacturers in the North, but there is a higher incidence in the North as a whole than in the South; and the rate among negroes in the South is higher than among whites.

Dublin gives 20 per 1,000 as the number of persons rejected each year by the life insurance companies on account of heart disease, whereas Hoffman puts the figure as 24.4. In a report recently made by the Ministry of Health for England and Wales, when 10,476,000 people between sixteen and forty-four years of age appeared on the panel, it was estimated on the basis of actual attack rates that 15,912 might develop rheumatic heart disease if the rate were 1.51 per 1,000 as it appeared to be. There is apparently a great difference between the rate in the companies and that on the panels. It must be remembered that the former is, in a sense, an unselected, the latter a selected sample of the community.

In industrial workers in general and in the investigation of garment workers in New York it was found by Scherescheswsky[14] that the rate was 20 per 1,000. Robinson and Wilson[15] arrived at the same

TABLE II

MORBIDITY

Chronic Valvular Disease in Various Places and Various Groups

	LOCATION	YEAR	POPULATION INVOLVED	HEART DISEASE		
				NO.	PERIOD	
Troops	U. S. Draft	1918	2,510,751	85,143	26.26	Love and Davenport, 1919[7]
	Agriculturists					
	U. S. Draft. North—White	1917–1918	10,005		34.15	Love and Davenport, 1919, Table 142, p. 281[7]
	U. S. Draft. South—White		10,571		24.60	" " "
	U. S. Draft. South—Negro		5,239		29.07	" " "
	Manufacturing					
	U. S. Draft. East		7,934		35.56	" " "
	U. S. Army	1926	1,000	15	15.00	Munly, Personal communication[8]
	Scotland	1916–1917	10,000	243	24.00	Report No. 23, Ministry of Health, 1924[9]
	Channel Islands	1901–1910			1.0	Kennedy[10]
	Yorkshire. East Riding	1901–1910			32.4	
	Wales. Carmarthen				2.0*	R. Miller, From report on physical examination of men of military age, i, 154, London, 1920[11]
	Cardiff				22.0*	
Insurance	Met. Life Insurance Co.				20.0†	L. I. Dublin, 1925[12]
	Prudential Insurance Co.	1915–1918			24.4†	F. L. Hoffman, 1920[13]
	England and Wales	1922	10,476,000‡	15,912‡	1.51	Report No. 23, Ministry of Health, 1924[9]
Industry	Garment workers				20.0	Schereschewsky, 1920[14]
	Various, Cincinnati				20.0	Robinson and Wilson, 1920[15]
	Food handlers				20.0	Harris and Dublin[16]
	Newsboys—New York City	1925	1,078	15	15.0	N. Y. Tuberculosis and Health Association, 1926[17]

* At age 18; †Of persons who apply for insurance; ‡Of persons actually insured. This equals the estimated number at ages 16-45.

figure in various industries in Cincinnati, and in a study of food handlers in New York by the Department of Health, Harris and Dublin[16] found exactly the same figure. In newsboys in New York studied by the New York Heart Committee the rate was 15 per 1,000.[17]

Lower rates are found among school children. (See Table III.) But this is not surprising for the ages involved are lower. Although the age of maximum incidence of rheumatic fever is five to seven years, all children destined to suffer from chronic heart disease have not yet become affected, nor indeed does rheumatic fever take its entire toll at so early an age. Even before fifteen years of age, it makes a difference whether the rates refer to entrants or to leavers; that for leavers in Glasgow, Bath, and London being twice as great as for entrants. In England there appears to be a difference also in school children between country and city, for the rate in the rural population is 2.6 per 1,000 and in the industrial 8.0, in a sample of 100,000 school children about thirteen to fourteen years old.

It appears then on the whole that among recruits, applicants for life insurance, and in industry, the incidence of chronic heart disease ranges from 15 to 35.56 per 1,000, the average being 20.8. There seems moreover to be a difference so far as locality and industry are concerned, for Kennedy gives the rate as low as 1 per 1,000 in the Channel Islands, against 32.4 in the East Riding Yorkshire, and in a country district in Wales as 2 per 1,000 against 22 in Cardiff.

Among school children the range of affection appears to be uncommonly wide, from 3.2 in Lanarkshire to 40 in Rochester, N. Y. Although the range is wide, in the sixteen localities nine fall between 7 and 16; two below, and five above these figures. It seems to be so great as to render unlikely the possibility of extracting from its consideration unified results. It is necessary to be quite certain that the methods of examination were uniform and the criteria for diagnosis fixed and well observed before it is possible to regard the data with confidence. Not to do so would cause the inference to be drawn that heart disease and its contributing etiological factors were prevalent in and affected the several school populations in variety and in numbers too widely different. I refrain therefore from averaging results, apparently so dissimilar.

There appears the fact, then, from a consideration of all the morbidity figures quoted so far that roughly 20 per 1,000 individuals are affected with heart disease in the adult population in the United States. Among school children so narrowly limited a rate cannot yet be given. The adult morbidity figures, however, harmonize even when obtained from such various sources. Is there a correspondence between the morbidity and mortality rates? If the figure for the death rate for 1920 in ages below forty years is recalled it was found to be 26 per 100,000; the morbidity rate in the draft was 26 per 1,000;

TABLE III

MORBIDITY

Chronic Valvular Diseases in Various Places Among School Children

LOCATION	YEAR	POPULATION INVOLVED	NO.	RATE PER 1000	REFERENCE
Lanark		32,000		3.2	G. A. Allan, 1926[18]
Philadelphia		23,671		6.3	Bd. Pub. Ed., 1924[19]
Transvaal		30,000		7.0	L. Leipoldt, 1920[20]
Glasgow*		240,000		7.0	G. A. Allan, 1926[18] (includes Aberdeenshire and Edinburgh)
Hempstead				8.2	L. Leipoldt, 1920[20]
Staffordshire		70,138		9.6	L. Leipoldt, 1920[20] (quoted from Priestly)
Aberdeenshire				10.0	G. A. Allan, 1926[18]
England and Wales		366,000		10.0	Report No. 23, Ministry of Health[9]
Glasgow*				10.0	G. A. Allan, 1926[18]
Edinburgh				13.0	G. A. Allan, 1926[18]
New York City		250,000		16.0	S. J. Baker, 1921[21]
Germany				23.0	L. Leipoldt, 1920[20] (quoted from unspecified German statistics)
Bath*				23.6	R. Miller, 1926[22]
London	1923	197,327	5,208	26.0	Annual Report, London C. C., 1923[5]
London*	1919	195,162	6,622	34.0	Report No. 23, Ministry of Health[9]
Rochester	1924		2,400	40.0	A. D. Kaiser, 1926[23]

				ENTRANTS 5-6 YR.		INTERMEDIATE 8 YR.		LEAVERS 12-14 YR.		
				M.	F.	M.	F.	M.	F.	
Glasgow				5.0				10.0		G. A. Allan, 1926[18]
Bath		8,000		10.0				23.6		R. Miller, 1926[22]
London	1919	195,162	6,622	25	22	33	36	38	49	Report No. 23, Ministry of Health[9]
						Total 34				
Rural	1924	100,000						2.6		R. Miller (quoted from Annual Report of Chief Medical Officer, Board of Education, 1924, London, 1925, 35), B. M. J., 1926[22]
Residential								5.9		
Industrial								8.0		

*For the rate for entrants, see below.

Hoffman's figure for rejections from the Prudential Insurance Company is not far removed from this; that in the industries, namely, 20 per 1,000, is somewhat lower. On the whole the morbidity rate is 100 times greater than that of mortality. In school children the morbidity rate in certain localities corresponds with the adult rate though it is in general much lower. It remains for further investigation to smooth out these disparities.

If we turn now from morbidity statistics of the population at large to consider the number of cases of heart disease which actually arise in medical practice the following figures are discovered. I confine myself to England and to the United States. In the London Children's Hospitals[24] the per cent is 31; Miller[25] gives 38 per cent; Church,[2] 57.5 per cent; St. Lawrence,[26] 61 per cent; Ingerman and Wilson,[27] 69 per cent; Cohn and Swift,[28] 94 per cent. If there are, according to Swift,[29] 175,000 cases of rheumatic fever in the country and if the average of 65 per cent (an average of St. Lawrence's, Ingerman's, and Wilson's rates) of cardiac involvement is accepted for the moment, there should be 113,750 cases of rheumatic heart disease. On the basis of the death rate, one-sixth of cases of heart disease die under forty years of age. Of the age of forty years, there will be discussion presently.

On the assumption that all patients with rheumatic heart disease and only patients with rheumatic disease die under forty, a not unreasonable assumption since the number of cases of syphilis under forty probably balance the number of cases of rheumatic disease above forty, the total cases of heart disease, seeing that cases of rheumatic disease number 113,750, should be six times as many, or 682,500. But the figure usually given for heart disease in the United States is 2,000,000, an estimate which is supported by having found the rate in various circumstances to be 20 per 1,000. There is then a serious error, a difference between 2,000,000 and 682,500, in the assumptions. Or again, if there are 113,750 cases of rheumatic heart disease, they represent only 5.7 per cent of the estimated total of 2,000,000; whereas it is known that one-sixth or 15 per cent of the cardiac population dies before the age of forty. The disagreement between 5.7 per cent of rheumatic cardiac cases and 15 per cent of cardiac deaths before forty is great. If total cardiac disability were 1,000,000 instead of 2,000,000, rheumatic cardiac patients would represent 11.3 per cent instead of 5.7 per cent of the total and would approach the figure for deaths under forty, 15 per cent, more closely. Just now it is impossible to say whether the error is due to too small an estimate in the number of rheumatic cases, to placing the involvement of the heart in rheumatic fever at too low a figure, or perhaps to too high an estimate of the number of persons believed to suffer from heart disease.

The next problem, after having outlined from mortality and morbidity statistics what might in all probability be the incidence of heart disease in the community, concerns the distribution of the cases affected both according to *age* and according to *etiological* groups. To make an analysis according to age commends itself especially on account of what has already been learned of the rising tide of chronic diseases which are naturally associated with older age groups. (See Table IV and Fig. 9.)

If, for instance, the age forty is taken as a dividing point it appears that in syphilis 19.7 per cent of the cases are under forty years of age, whereas 80.1 are over. And if 957 cases of degenerative heart disease

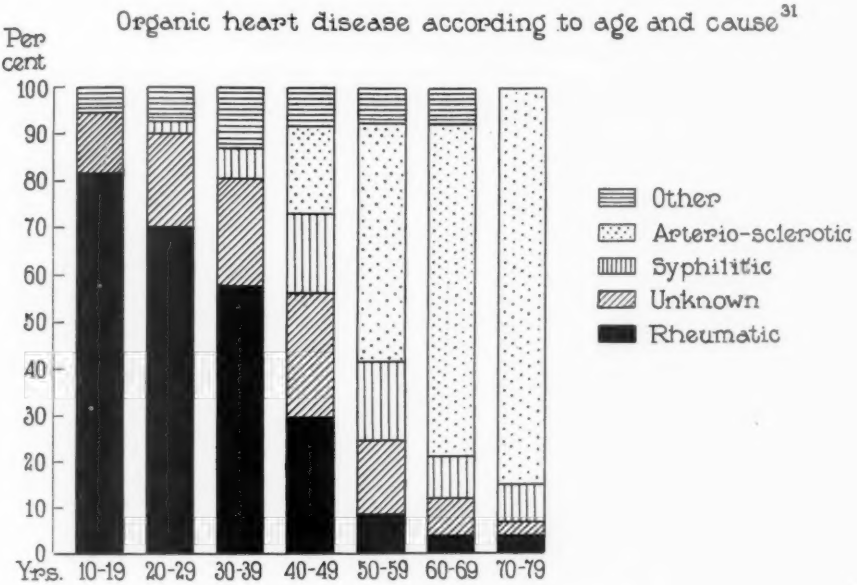

Fig. 9.

are considered, again with age forty as the dividing point, 6.0 per cent occur before the age of forty and 93.2 above. Syphilis and the degenerative diseases combined occur above forty to the extent of 86.6 per cent. If, however, instead of muscular or degenerative diseases we study 2614 cases of valvular disease, 75.41 per cent occur under age forty and 24.73 per cent above this age. From the point of view of mortality rates, age forty seems likewise to be a useful point of division, for here it will be remembered 26 per 100,000 or 14.6 per cent of the total cases die before age forty in a total death rate of 178, a ratio of 1 to 6.85. There appears now to be a difficulty like that which was encountered before, for these facts seem to indicate that 33.70 per cent (the average 19.7 + 6.0 + 75.41) of clinic patients both in Germany, the United States, and England are less than forty

TABLE IV

DISTRIBUTION OF MUSCULAR AND VALVULAR DISEASES OF THE HEART IN RELATION TO AGE FORTY

MORBIDITY	NO.	PER CENT BEFORE AGE 40	PER CENT AFTER AGE 40	
Syphilis		13.6	86.4	Romberg[30]
Syphilis	91	16.3	83.4	Wyckoff and Lingg[31]
Syphilis		29.3	70.7	Stokes[32]
		Av. 19.7	80.1	
Arteriosclerosis	234	0.4	99.5	Wyckoff and Lingg[31]
Muscular degeneration	723	11.6	87.0	Romberg[30]
Total	957	Av. 6.0	Av. 93.2	
Valvular heart disease	399	59.2	40.8	Romberg[30]
Valvular heart disease	670	73.68	27.32	Romberg[30]
Valvular heart disease	210	63.55	37.25	Schnitt[33]
Rheumatic heart disease	449	83.2	16.8	Wyckoff and Lingg[31]
Rheumatic heart disease	201	68.5	31.5	Fatianoff[34]
Rheumatic heart disease		65.3	34.7	Leuch[35]
Rheumatic heart disease	494	95.6	3.8	Church[2]
Rheumatic heart disease and chorea	191	94.3	5.7	Mackie[36]
Total	2614	Av. 75.41	24.73	
MORTALITY				
Organic disease of heart		14.6	85.4	International List of Causes of Death No. 90

years old, whereas the mortality rate below forty years is only 15 per cent. The reason for this difference as before is difficult to understand. Wyckoff and Lingg have attempted to explain it; I shall return to this point later.

The age distribution then appears to give a clue to the nature of the diseases with which we must deal. It appears that the valvular diseases are predominantly the diseases which occur before the age of forty, the muscular diseases and syphilis afterward.

There is another way of approaching this matter of the division at the age of forty. It is well known that infection from rheumatic fever has its point of maximum incidence before age ten. It is true that this age is variously given, being placed at age six and one-half (Ingerman and Wilson[27]) and at age seven (Miller-Poynton, quoted by Ingerman and Wilson[27]). But that the turn of the first decade of life is the important one from the point of view of onset is seen also by the sharp rise in incidence that takes place between entrants and leavers in British schools.

Infection due to rheumatic fever occurs, of course, at other age groups, but it is here at a maximum. Church[2] in a study of 943 cases of rheumatic fever gives the age incidence under ten as 13.99 per cent; under twenty, as 57.57 per cent; and under thirty as 83.23 per cent. It is difficult to assign a figure to represent accurately the duration between onset and affection. There seems to be, relatively speaking, a small amount of data on the subject. But Coombs[37] states it as a fact that 66 per cent of cases of heart disease following on rheumatic fever occur between the ages of five and fifteen. Thayer[38] gives the same percentage below twenty. Mackie's[36] cases below twenty were 55 per cent. St. Lawrence[39] cites the history of seven cases in which rheumatic fever preceded the detection of valvular disease at intervals ranging from 13 to 72 months. The figures for the seven cases are 13, 26, 41, 45, 53 and 72 months; the average being 41.6 months. In the seventh case heart disease was present before the appearance of the more usual rheumatic symptoms.

Among 25 cases of mitral stenosis, Mackie reports that the lesion was developed in twenty-four months in 22, but that it required five and one-half, six and one-half and five and two-thirds (chorea) in 3 additional cases. It may take then one to six years for the cardiac lesion to form. Meanwhile manifestations of rheumatic disease may be quite absent. Next, the length of time before heart failure begins, Romberg[30] gives as approximately seven years, in 102 cases of valvular heart disease in his Leipzig clinic. The stage of heart failure itself may on the average last, as he shows also in a study of 172 cases in Leipzig clinic, four and eight-tenths years. If now these three periods are summed up,—(1) the period from the beginning of the infection to the establishment of the chronic valvular lesion, say one

to eight years, the average about four years; then (2) from this point to the onset of heart failure, say about seven years; and finally (3) from this point to death, say about four years, the total period is somewhere in the neighborhood of fifteen years. On the assumption that Church's figures and those of Ingerman and Wilson[27] and Miller and Poynton are correct, and that the ages five to fifteen embrace the usual period for infection from rheumatic fever, the total course of the disease will have been run by the ages twenty to thirty years. Or if the higher figures in Church's table are to be considered, namely, those which assign 25 per cent of cases of rheumatic fever to the third decade, the twenty to thirty years age group, the disease will have run its course between the ages of thirty-five and forty-five. This calculation again permits the selection of age forty as an important point in a consideration of chronic heart disease for it has now been shown that this age is significant in the natural history of rheumatic fever, that it is moreover important in morbidity and mortality statistics.

In view of the great significance that rheumatic fever has in the early ages of life it becomes important to obtain some estimate of the number of cases in a population which suffers from this disease. Reference has already been made to Swift's[29] statement that there are 175,000 cases in the United States. To obtain data for this is difficult for rheumatic fever has rarely been a notifiable disease. (See Table V.)

There was a period, however, from 1891 to 1895 when the disease was notifiable in Norway. At that time it was found in a population of 2,020,840 (1900 Census) that among 1,302,298 (64.4 per cent) above

TABLE V

INCIDENCE OF RHEUMATIC FEVER*

Norwegian, English and Welsh Practitioners, City of Ulm

	YEAR	AGE	POPULATION		ATTACK RATES PER 1000		CASES	
			MALES	FEMALES	MALES	FEMALES	MALES	FEMALES
Norway	1891–1895**	15+	604257	698041	2.07	1.9	6281	6771
			Total 1,302,298***				Total 13,052†	
Practitioners	1922	16–24			1.995			
Ulm	1883–1900	10–20			1.93			
Practitioners	1922	All	57998	32893	0.88	1.76‡	51	58
			Total 90.891††				Total 109	
Ulm§	1906	All			1.75	1.24		

*Compiled from pp. 64-65 Reports on Public Health and Medical Subjects. No. 23. Ministry of Health, 1924.

**Years of compulsory notification.

***64.4 per cent of total population of 2,020,840 in 1900 Census.

†Age 15+ was 81.7 per cent of total notified (15978).

††Total population at risk 12,633,000.

‡Females equal twice the males. Half the females at susceptible age, 16-24.

§F. Prinzing, Handbook Medical Statistics, 1906, p. 340

the age of fifteen, 13,052 cases developed. The male population was 604,257, the attack rate 2.07 and the cases of rheumatism 6281. The female population was 698,041, the attack rate 1.9, and the cases 6771. The average attack rate equals 1.98. In the Practitioner's Inquiry carried out under the Ministry of Health[9] in a certain selected portion of England and Wales, 90,891 persons come on the panel of a population of 12,633,000. Among these 51 males and 58 females developed the disease. The attack rates were 0.88 for males and 1.76 for females. For the age period sixteen to twenty-four, approximately like that in the Norwegian data, the attack rate was 1.995. There are figures for the city of Ulm during the years 1883 to 1900 which give attack rates for the ages ten to twenty as 1.93.

Swift[29] on the basis of mortality data for 1916 in the United States Registration Area says that the combined figures for rheumatic infection show a rate of 6.7 per 100,000. If as he believes the death rate represents 4 per cent of the cases affected there should be in the United States between 150,000 and 175,000 cases of rheumatic fever. On the same basis, the death rate being 6.7 per 100,000 and representing 4 per cent of the cases, the attack rate in the United States equals 1.67 per 1,000. It will be seen then that a comparison of the attack rates of the Norwegian, Ulm, and the Practitioner's Inquiry presents a certain degree of correspondence; the Norwegian figure for both sexes being 1.98 (all ages above fifteen), the British figure being 1.32, the Ulm figure being 1.45, and Swift's 1.67.

It is not my purpose to discuss all the factors which make for the occurrence of rheumatic fever. The problem of possible bacterial agents has, as you know, engaged the attention of investigators for many years. I need go into no further detail than to recall the fact that there is no general agreement on which microorganism is the efficient cause nor indeed whether the cause is a microorganism at all.

The relation of damp and wet and cold is also often mentioned, especially in the older literature. There are two aspects of this phase of the problem, seasonal and geographical. It has been explored by many older writers, reviewed carefully by Pribram[40] and more recently by Newsholme,[41] Greenwood and Thompson,[6] Young,[42, 43] the Practitioner's Inquiry,[9] and Miller.[11] Pribram, Newsholme, and Greenwood and Thompson have opposed the idea of a relation of rainfall to the occurrence of rheumatic fever; Garrod on the whole favored it as did Young, the Practitioner's Inquiry, and Miller. Opinion then is still divided. Miller reports that of 196 cases, 122 or 62.2 per cent occurred in damp rooms. He presents data to show that among persons who live in them or in basements or in ground floor rooms without cellars, the liability to the disease increases. The Practitioner's Inquiry[9] concludes that dampness has a higher correlation with acute rheumatism than with any other rheumatic disease. It was also shown

that if the attack rates from rheumatic fever and rheumatism of the heart for all England and Wales were placed at 100, the attack rates for Lancashire may be placed at 159, the highest in England. Norwich, in East Anglia, is on the contrary exceptionally free from rheumatic diseases. Lancashire situated in the Northwest, has relatively the higher rainfall.

Some day perhaps we may recall in this connection Pettenkoffer's idea that the height of the ground water in Munich was related to the occurrence of typhoid fever.

A discussion of rheumatic fever is not complete without reference to the possibility of its infectious nature. Church[2] quotes Friedlander as having seen 12 cases in the same house in Leipzig in three years. He also quotes Edelfson as having counted 728 cases in 492 houses.

More recently a number of new reports have been published on its familial and hereditary aspects. (See Table VI.) Coombs[37] gives 50 per cent as the incidence in families, in which there were cases in addition to his patients. St. Lawrence[45] in a hundred families gives the figure as 29 per cent for rheumatic heart disease; Miller[22] quotes Coates and Thomas as giving 47 and 37 per cent affected, in two series, and Morrison, as giving 48 per cent; Faulkner and White[46] give the rate as 35.5 per cent. In the control families of healthy individuals, the per cent falls to 16. In rheumatic families, if I may so call them, there were 8 to 10 per cent of exposed persons infected as against 1 to 2 per cent in the population at large, and in the families of healthy controls only 2.95 per cent. These figures are striking enough to stimulate more searching inquiry in this direction. It is a phase of the problem which was not without interest in the study of tuberculosis, and is now the subject of research in lobar pneumonia.

It is not surprising that with a disease incidence as large as that in rheumatic fever much thought has been expended on the possibility of remedying this situation. From the point of view of the public health to institute a serious effort in this direction is eminently desirable. On account of the frequent association of other affections, more especially that of the tonsils, with this condition attempts have been made to modify the incidence and course of rheumatic fever by attention to this source of infection. Unfortunately much information does not yet exist on the subject.

There are, however, several series of cases, beginning in the year 1908, in which reports have been made on the effect of operation on the tonsils. (See Table VII.) It is perhaps important to distinguish the cases in which removal of the tonsils was complete, that is to say the cases in which the tonsils were completely enucleated and those in which the enucleation was incomplete. There were 391 cases observed before and after operation. The rheumatic manifestations for which the operations were performed recurred in 49.6 per cent of these. This

TABLE VI

RHEUMATIC DISEASES

Familial and Hereditary Aspects

FAMILIAL	DISEASE	NUMBER PATIENTS	NUMBER STUDIED		NO. MEMBERS IN SAME FAMILY AFFECTED	TOTAL FAMILIES AFFECTED		AFFECTED PERSONS DISCOVERED		PERSONS UNAWARE OF DISEASE		REMARKS
			FAMILIES	PERSONS		NO.	%	NO.	%	NO.	%	
St. Lawrence[45]	Heart disease		100	480	2 or more	29	29	38	8.0*	27	71	Usual 1–2%*
	Acute rheumatic fever	100	100	480	2 or more	24	24	49	10.0*			Usual 1%*
	Chorea		100	480	2 or more	3	3	8	1.6			
Ingerman and Wilson[27]	Rheumatism	185				74 Parents	40					
						51 B & S†	28					
Miller[22]	Rheumatic infections	44				21						
(from Coates and Thomas)		32				12						
(from Morrison)		54				26						
Coombs[37]							50					
Faulkner and White[46]	Rheumatic affections	200	200	1235*	2 or more	71	35.5	108	8.79			642 examined*
	Healthy controls	75	75	474*	2 or more	12	16.0	13	2.95			366 examined*

HEREDITARY	PARENT AFFECTED						SIBLINGS AFFECTED
	NO. PATIENTS	NUMBER	PER CENT	FATHERS	MOTHERS	BOTH	PER CENT
Faulkner and White[46]		332	8.9				8.66
Report 23[9] Males			24.0	13	21	8	
Females			43.0	7	15	2	

*Compare with statement on same line under remarks.
†B & S—Brothers and sisters.

TABLE VII

TONSILLECTOMY

Its Effect on the Occurrence of Rheumatic Manifestations

DATE	AUTHOR	NO. CASES TOTAL	*With Tonsillectomy* NO.	PER CENT	NO RECURRENCE NO.	PER CENT	WITH RECURRENCE NO.	PER CENT	*Without Tonsillectomy* NO.	PER CENT	NO DEVELOPMENT OF MANIFESTATIONS NO.	PER CENT	WITH DEVELOPMENT OF MANIFESTATIONS NO.	PER CENT	REMARKS
Complete Tonsillectomy															
1908	Rosenheim[49]		10		10	100	0	0							
1911	Archibald[50]	7	7		5	71.4	2	26.8							
1915	Young[51]	21	21		6	28.6	15	71.4							
1917	Crewe, Watkins and Rothholz[52]	49	49		28	56.3	21	43.7							
1920	St. Lawrence[26]	85	85		54	63.5	31	36.5							
1923	Hunt and Osman[47]	144	66		31	47	35	53	78		45	58	33	42	All cases
		(99)	(50)				(23)	(46)	(46)				(15)	(33)	After first attack
		(48)	(16)				(12)	(75)	(32)				(18)	(56)	After later attacks
1924	Ingerman and Wilson[27]	167	70		17	24	53	76	97		19	19.6	78	80.4	
1924	Dulaney[53]		22		22	100.0	0	0							
1926	R. Miller[25]	133	45		18	40	27	60	(83)						
1926	R. Miller (A. P. Thompson)[48]	16	6		6		10	62.5							
1926	Mackie[36]	299	80		46	57.5	34	42.5	207		82	39.7	125	60.3	After first attack
			12		0	0									Before first attack
Totals			483		255	52.8	228	47.2	382		146	38.2	236	61.8	
1926	Kaiser[23]	2400	1200						1200				128		Rheumatism
Partial Tonsillectomy															
1921	St. Lawrence[26]	9	9		1		8								
1924	Ingerman and Wilson[27]	18	18		4		14								
Totals		27	27		5	18.0	22	82.0							

figure is low rather than high, for recurrence involves consideration of the period of time after operation during which observations were carried on, as it has been found that the percentage rises with time. This point is especially important for in several instances enumerated in this table the duration of observation has been short, a matter of months rather than of years. In connection with these 391 cases, 2,400 cases studied by Kaiser[23] should be mentioned. It is unfortunate that Kaiser has not yet published analyses of his large number of carefully studied cases in such detail as to make it possible to enter the results in a table such as this. In order to be able to do this, it is of course necessary to be able to follow the course of the disease in each individual. Few investigators have as yet appreciated the importance

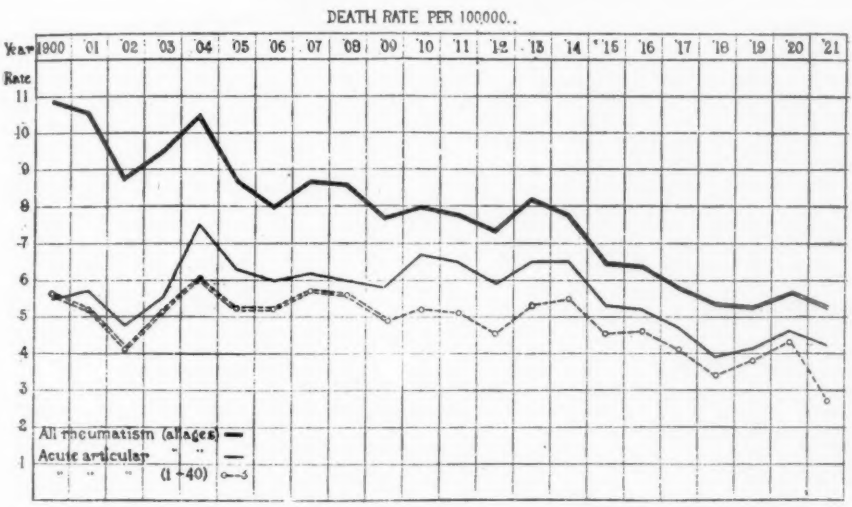

Fig. 10.—Death rate from all rheumatism, and from acute rheumatic fever in New York State, 1900-1921.[54]

of this method of presenting data, especially outside the United States. In the group in which enucleation was incomplete there were 27, among these 22 (82 per cent) recurred.

There have been reported several groups of cases in which no operations on the tonsils were performed. These serve as controls. Of well studied cases, 175 may be mentioned, among which rheumatic manifestations developed in 111 or 64 per cent. The largest series of cases studied from this point of view is Kaiser's.[23] Twelve hundred cases were observed. Of choreic manifestations there occurred 7, of rheumatic 128, and of cardiac 52. But among the cases operated upon there were 8 instances of choreic, 129 of rheumatic and only 44 of cardiac manifestations; that is to say there were more rheumatic and choreic manifestations in those operated upon than in the so-called controls. It is necessary to speak of manifestations rather than of

cases for the number of cases which the manifestations involved is not given. The most signal advantage of the operation seems to have been in the cases of tonsillitis for here among the operated there were only 64 cases as against 586 in the nonoperated. Unfortunately the effect of operation on the matter of recurrence, the essential object of study, is not deducible from Kaiser's report. On the whole then, it cannot

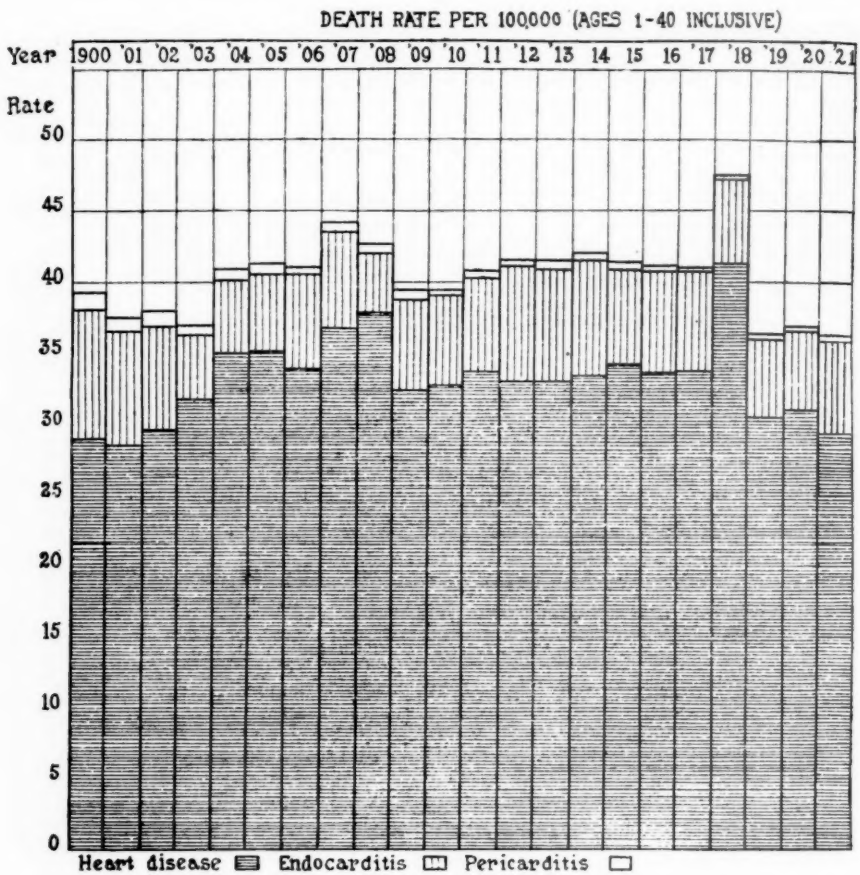

Fig. 11.—Specific death rates (ages one to forty years inclusive) for heart disease, endocarditis and pericarditis in New York State, 1900-1921.[54]

be said that the results of this therapeutic measure are satisfactory, recurrence taking place in 50 per cent of the cases. When series of cases reported by individuals are considered, attention must be paid to St. Lawrence's view[39] that especially in cases in which chorea is not a factor the performance of tonsillectomy is an extremely important measure. To discuss each series of cases is important but impossible here. Miss Lingg, my associate in the Heart Committee in New York, is at present engaged in making a complete analysis. Interpretation

is difficult, for not only as has already been said must time of observation be taken into consideration but also the time of operation in relation to the onset of rheumatic disease and especially the relation to first or second attacks. Although from Kaiser's observations tonsillectomy seems to make no difference from important points of view, this method of therapeutics must nevertheless be carefully pursued precisely for the reason stated. It is urgently desired that observers record their cases in such a way as to make it possible to deduce what has actually been the course of events in their patients.

Of other means of preventing and relieving rheumatic fever, only a few words need be said. The use of drugs, as effective agents of cure, must unfortunately be dismissed. Careful investigators are unanimous in their opinion that no hope lies in the direction of the use of those which have so far been proposed.

But that, as in the case of tuberculosis, something may be accomplished by prolonged and complete rest, the reports of Swift[54] more recently published indicate clearly. Coleman[55] has insisted on this point and has illustrated his contention with telling case reports. Experiences like these emphasize the fact that in order to duplicate them, facilities in the way of beds in hospitals and in convalescent institutions properly supervised are requisite. They tend also to lend point to the general observation that treatment of patients in private, in the economically more self-sufficient walks of life, is attended by prolongation of activity and of life. That the failure to provide such facilities possibly shortens usefulness and life will appear in considering the curves of Wyckoff and Lingg.

Aside from the analysis which has already been made showing the very partial success of tonsillectomy on the course of rheumatic infection, a study of the death rate curve in New York State made by Swift[54] shows that no substantial change has occurred in ages below forty either in endocarditis, in pericarditis or in organic heart disease. (See Figs. 10 and 11.) His curves for rheumatism and for acute rheumatic fever show a persistent fall and encourage one in the pursuit of the therapeutic measures which have been described.

(To be concluded in April issue)

AN ELECTROCARDIOGRAPHIC STUDY OF EXPERIMENTAL HEART DISEASE*

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DISEASE of the myocardium has been produced experimentally by many workers and a review of the literature was given by I. Chandler Walker in 1911.[1] A method was first described by Fleisher and Loeb,[2] which consists in the single intravenous injection in rabbits of 0.2 c.c. of a 1:1000 solution of adrenalin and 25 mg. of caffeine sodium benzoate. Scott Johnson combined the experiments of Fleisher and Loeb and will report his results in another paper. We may, however, state that he could produce by means of this method a gross myocardial lesion after a period of from twelve to twenty-one days in over 90 per cent of his rabbits. He found the lesion occurring not only in the ventricle but also in the left auricle, from which it extended to the base of the left ventricle. The papillary muscles were always involved. He also attempted to produce a suppurative lesion in the myocardium by multiple intravenous injections of living Staphylococcus aureus cultures in rabbits previously treated with caffeine and adrenalin. He could show that acute vegetative endocarditis and mural thrombi developed in rabbits receiving one intravenous injection of caffeine and adrenalin followed by one or more intravenous injections of living Staphylococcus aureus.

In the course of these experiments it was suggested by Dr. Leo Loeb that some of the animals in which myocardial lesions had been produced should be used for an electrocardiographic study, with the hope of obtaining a method whereby electrical changes in the heart muscle could be compared in both normal and pathological hearts and under experimentally and microscopically controlled conditions. To this end the following experiments were carried out on rabbits, electrocardiograms being taken by means of copper wire electrodes attached to the animals' legs for the various leads.

Instead of injecting the adrenalin and caffeine separately at different time intervals as did Fleisher and Loeb, the adrenalin and caffeine were mixed together with sterile water so that 1 c.c. of the aqueous solution contained 0.2 c.c. of a 1:1000 solution and 25 mg. of caffeine sodium benzoate. Thirteen rabbits were given one injection of the above dose. This was followed by four successive injections of 1 c.c. of a forty-eight-hour broth culture of Staphylococcus aureus. These

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were started from six to twelve days after the original injection of caffeine and adrenalin and were continued at forty-eight-hour intervals. Eight of the rabbits received the injections intravenously and five intrapericardially. As controls twelve rabbits were used, each receiving only four injections of 1 c.c. of a forty-eight-hour broth

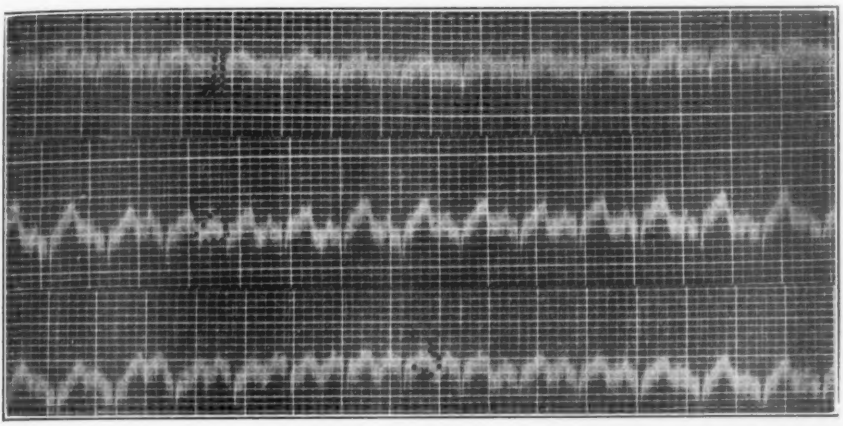

Fig. 1.—Example of curves of each lead before the administration of adrenalin and caffeine sodium benzoate.

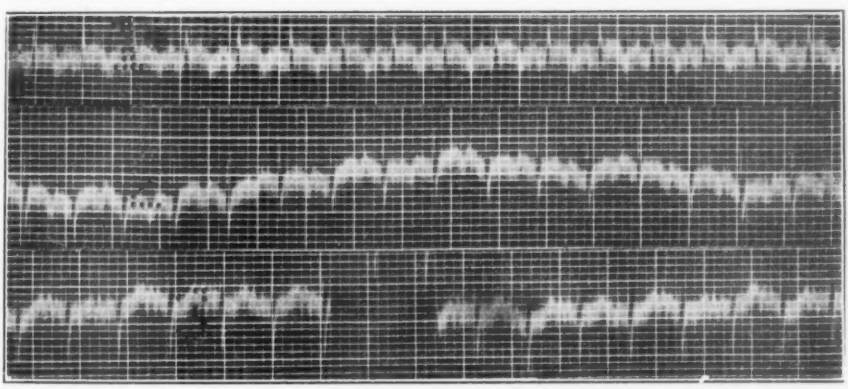

Fig. 2.—Example of curves of each lead fourteen days after the administration of adrenalin and caffeine sodium benzoate.

culture of Staphylococcus aureus at forty-eight-hour intervals, six intravenously and six intrapericardially. Electrocardiograms were taken at the beginning of the experiment and frequently thereafter, the galvanometer string being standardized for all three leads as the curves were taken (see Table I). In from twelve to seventeen days after the caffeine and adrenalin injection the animals were killed by a blow on the head and the gross and microscopical pathological findings were noted.

TABLE I

RABBITS RECEIVING CAFFEINE AND ADRENALIN PRIOR TO INJECTIONS OF STAPHYLOCOCCUS AUREUS CULTURES

NO.	METHOD OF STAPHYLOCOCCUS INJECTION	NO. OF DAYS AFTER INJECTION	E. K. G. FINDINGS						PREPONDERANCE	PATHOLOGICAL CHANGES IN THE HEART
			P	P-R	QRS	T-WAVE				
						LEAD I	LEAD II	LEAD III		
2	I.V.	0	N	.08″	N	I	U	U	O	C. and A. myocarditis; hyperemia of pericardium
		1	N	.08″	N	U	U	U	O	
		2	N	.08″	N	U	U	U	O	
		3	N	.08″	N	D	U	U	O	
		4	N	.08″	N	D	U	Di	O	
		6	N	.08″	N	D	I	Di	left	
		12	N	.08″	N	D	U	U	O	
3	I.V.	0	N	.08″	N	U	U	U	O	None
		1	N	.08″	N	U	U	U	O	
		2	N	.08″	N	U	U	U	O	
		3	N	.08″	N	U	U	U	O	
		4	N	.08″	N	U	U	U	O	
		6	N	.08″	N	U	U	U	O	
		12	N	.08″	N	U	U	U	O	
4	I.V.	0	N	.08″	N	U	U	Di	O	C. and A. myocarditis; mitral and mural endocarditis
		1	N	.09″	N	U	U	U	O	
		2	N	.08″	N	U	Di	D	O	
		3	N	.09″	N	U	Di	D	O	
		4	N	.09″	N	Di	Di	D	O	
		6	N	.08″	N	Di	Di	Di	O	
		14	N	.08″	N	Di	U	U	O	
5	I.V.	0	N	.08″	N	U	U	U	right	C. and A. myocarditis; mural thrombi
		1	N	.08″	N	U	U	U	"	
		2	N	.08″	N	Di	Di	Di	"	
		3	N	.08″	N	D	D	Di	"	
		4	N	.08″	N	D	D	Di	O	
		6	N	.09″	N	D	D	Di	O	
		14	N	.08″	N	D	D	Di	left	

NOTE:—I.V., intravenously; I.P., intrapericardially; N, normal; U, up; D, down; Di, diphasic; I, isoelectric; O, initial electrocardiogram; C. and A., caffeine and adrenalin.

TABLE I—CONT'D

NO.	METHOD OF STAPHYLOCOCCUS INJECTION	NO. OF DAYS AFTER INJECTION	E. K. G. FINDINGS						PREPONDERANCE	PATHOLOGICAL CHANGES IN THE HEART
			P	P-R	QRS	T-WAVE				
						LEAD I	LEAD II	LEAD III		
6	I.V.	0	N	.08″	N	U	U	U	O	C. and A. myocarditis; mitral endocarditis
		1	N	.08″	N	I	U	U	O	
		2	N	.08″	N	D	Di	Di	O	
		3	N	.07″	N	I	Di	I	right	
		4	N	.08″	N	I	Di	D	O	
		16	N	.08″	N	U	U	U	O	
7	I.V.	0	N	.09″	N	U	U	U	right	C. and A. myocarditis; mural thrombi
		1	N	.09″	N	U	U	I	"	
		2	N	.08″	N	U	U	U	"	
		3	N	.08″	N	U	U	U	"	
		4	N	.08″	N	I	U	U	"	
		6	N	.07″	N	I	U	U	"	
		16	N	.08″	N	D	U	U	"	
8	I.V.	0	N	.08″	N	U	U	Di	O	C. and A. myocarditis; mitral endocarditis and mural thrombi
		2	N	.08″	N	D	Di	Di	left	
		4	N	.08″	N	D	Di	U	"	
		15	N	.08″	N	D	U	U	"	
9	I.V.	0	N	.08″	N	U	U	U	O	C. and A. myocarditis; mural thrombi
		3	N	.08″	N	I	U	U	O	
		4	N	.08″	N	I	U	U	O	
		15	N	.08″	N	I	U	U	O	

NOTE:—I.V., intravenously; I.P., intrapericardially; N, normal; U, up; D, down; Di, diphasic; I, isoelectric; O, initial electrocardiogram; C. and A., caffeine and adrenalin.

TABLE I—CONT'D

NO.	METHOD OF STAPHYLOCOCCUS INJECTION	NO. OF DAYS AFTER INJECTION	E. K. G. FINDINGS						PREPONDERANCE	PATHOLOGICAL CHANGES IN THE HEART
			P	P-R	QRS	T-WAVE				
						LEAD I	LEAD II	LEAD III		
10	I.P.	0	N	.08″	N	U	U	U	O	C. and A. myocarditis; hyperemia of pericardium
		2	N	.08″	N	D	U	U	O	
		3	N	.08″	N	U	U	U	O	
11	I.P.	0	N	.08″	N	I	U	U	O	C. and A. myocarditis; fibrinopurulent pericarditis
		3	N	.07″	N	I	Di	Di	O	
		4	N	.08″	N	I	Di	Di	O	
		5	N	.08″	N	D	I	Di	O	
		7	N	.08″	N	D	Di	U	O	
12	I.P.	0	N	.08″	N	I	U	I	left	C. and A. myocarditis; hyperemia of pericardium
		2	N	.09″	N	I	U	U	"	
		3	N	.07″	N	I	Di	Di	"	
		4	N	.08″	N	I	Di	Di	"	
		10	N	.08″	N	D	U	U	"	
14	I.P.	0	N	.08″	N	U	U	U	O	C. and A. myocarditis; fibrinopurulent pericarditis
		2	N	.08″	N	D	U	U	O	
		3	N	.08″	N	D	U	U	O	
		4	N	.08″	N	D	D	D	O	
		10	N	.08″	N	D	U	U	O	
16	I.P.	0	N	.08″	N	U	U	U	O	C. and A. myocarditis
		2	N	.09″	N	I	U	U	O	
		3	N	.08″	N	Di	U	U	O	
		4	N	.08″	N	I	U	U	O	
		5	N	.08″	N	I	U	U	O	
		14	N	.08″	N	U	U	U	O	

NOTE:—I.V., intravenously; I.P., intrapericardially; N, normal; U, up; D, down; Di, diphasic; I, isoelectric; O, initial electrocardiogram; C. and A., caffeine and adrenalin.

In twelve control animals there were no changes in the electrocardiograms when Staphylococcus aureus was injected alone. This was true both with intrapericardial and intravenous injections. In interpreting the electrocardiograms attention was directed to the P-wave, P-R interval, QRS complex, T-wave, and the preponderance. While four of the six control rabbits injected intrapericardially showed a fibrinopurulent pericarditis, there was in only one animal evidence of a myocardial or endocardial involvement. In this case a very small abscess of 1 mm. in diameter was found in the left ventricle.

The changes resulting from these injections are recorded in Table I. The outstanding features can be summarized as follows:

1. Nine rabbits which had a normal Lead I before the experiment, all showed some change in the T-wave after caffeine and adrenalin injections (4, 5, 6, 7, 8, 9, 10, 14, and 16). This change was either isoelectric, diphasic or consisted in inversion. These changes were not constant when once produced, the curves sometimes returning to normal or nearly so after several days (6, 10, and 16).

2. In Lead II, eight of twelve rabbits at some time showed a deviation of the upright T-wave and four showed no change whatsoever (2, 4, 5, 6, 8, 11, 12, and 14). In six of these (2, 4, 6, 8, 12, and 14) the T-wave returned to the upright position in from six to sixteen days. None of the twelve rabbits had any initial T-wave changes in Lead II.

3. Six of twelve rabbits in Lead III exhibited changes after caffeine and adrenalin injections (2, 5, 6, 7, 11, and 14). In three rabbits in Lead III (4, 8, and 12) there was an initial T-wave change and two of them (4 and 12) showed some further change after caffeine and adrenalin.

4. In one rabbit (3) no change was noted in the T-wave throughout the time of observation and at autopsy the heart was found to be entirely normal.

5. Twelve of thirteen rabbits had a myocardial lesion.

6. No change could be made out in the P-wave, P-R interval, or QRS complex in any of the rabbits before or after caffeine and adrenalin.

7. In four rabbits (2, 5, 6, and 8) a change was noted in regard to preponderance.

On the basis of these observations there can be little doubt of the occurrence of definite changes in the electrocardiograms as a result of the caffeine and adrenalin injections. These changes occur chiefly in the T-wave in Leads I and II. We may further conclude that the electrocardiographic changes are due to the caffeine and adrenalin myocarditis, inasmuch as all the rabbits exhibited a change at some time following the caffeine and adrenalin injection while the controls showed no changes even though they were injected with Staphylococcus aureus intravenously or intrapericardially. This we believe

tends to disprove that the lesion is spontaneous, as has been held by other workers on this subject.[3]

There is an apparent disparity between the electrocardiograms and the pathological findings in the heart at autopsy. In eight rabbits (2, 4, 6, 8, 10, 12, 14, and 16) the T-wave, originally altered, returned to normal while an anatomical lesion persisted. This fact can be explained if we consider that the lesions in the heart produced by caffeine and adrenalin vary greatly in intensity in different cases. In some hearts the lesion is slight, in others moderate, and in some quite extensive. Furthermore, the heart lesion undergoes a change from day to day, the lesion progressing up to a certain time and then receding. We may foresee that these factors will influence the character of the electrocardiogram.

From the gross appearance of the heart it is difficult to say whether or not there is an hypertrophy. Other workers[1, 3] conclude that all rabbits showing myocarditis also exhibit hypertrophy. Pathologically we were able to confirm the work of Fleisher and Loeb[2] that microscopically there is an hypertrophy of the muscle fibers of the heart. This was true in all of our experiments, and we regard the evidences of changes in preponderance in the electrocardiogram as possibly due to this factor. Why it did not occur in more rabbits in the experiment remains to be explained.

No changes in the conduction mechanism were noted. With the type and location of the myocarditis one would not expect such a change. The pathological examinations, however, did not include observations on the bundle of His.

The hearts of all the animals directly after death at the time of examination were still beating and upon observation it was seen that the myocarditic area contracted sluggishly or not at all, as compared with the contraction of the normal part of the left ventricle. Since in noncontracting muscle one would not expect a change in the electrical potential, the possibility must be considered that quantitative changes in the contraction of the left ventricle alter the direction of the spread of negativity and the deviation of the T-wave. In all cases the left and right ventricles of the heart appeared to contract simultaneously.

Table II correlates the changes in the T-wave with the location of the pathological alterations in the muscle and the character of contraction of the left ventricle. In the table it will be noted that the upper half of the left ventricle was involved in eleven instances, the middle anterior third is one. The auricular lesion is found on the left side, and as a general rule if extensive is accompanied by a gross lesion of the upper half of the left ventricle. Three of the rabbits (5, 8, and 14) had an extreme myocarditis of the left ventricle and in

TABLE II

RELATION OF CHANGES IN THE T-WAVE TO MUSCULAR CONTRACTION AND LOCATION OF THE AREAS OF MYOCARDITIS

NO.	CONTRACTION OF LEFT VENTRICLE	PAPILLARY MUSCLE	LOCATION OF MYOCARDITIS		E. K. G. CHANGES IN LEAD II
			UPPER LEFT VENTRICLE	LEFT AURICLE	
2	normal	+++	++	none	I on 6th day—U on 12th day
4	sluggish	+++	+	+++	Di on 2nd day—U on 14th day
5	sluggish	+++	+++	+++	Di on 2nd day—D on 14th day
6	sluggish	+++	++	none	Di on 2nd day—U on 16th day
7	sluggish	+++	++	+	None
8	sluggish	+++	+++	+++	Di on 2nd day—U on 15th day
9	sluggish	+++	++	none	None
10	normal	+++	++	+	None
11	sluggish	+++	++	none	Di on 3rd day—also on 7th day
12	normal	+++	++	none	Di on 3rd day—U on 10th day
14	sluggish	+++	+++	+++	D on 4th day—U on 10th day
16	normal	+++	+	+	None

NOTE:—I, isoelectric; U, up; D, down; Di, diphasic; +, slight; ++, moderate; +++, marked.

each case it was found to contract sluggishly, there always being a marked change in the T-wave in Lead II. Seven rabbits (2, 6, 7, 9, 10, 11, and 12) showed a moderate, gross myocardial lesion of the left ventricle, involving the upper half of the left ventricle in six instances and the anterior middle third in one instance (7). The myocarditic area contracted sluggishly in four of these seven rabbits and normally in three. The T-wave was diphasic or isoelectric, but never inverted, in four of these cases (2, 6, 11, and 12). In three there was no change in the electrocardiogram. The remaining two rabbits (4 and 16) showed only slight myocarditis of the left ventricle, one showing normal and the other sluggish muscle contraction. In only one of these rabbits T-wave changes were observed.

These data allow us to conclude that a moderate myocardial lesion may exist without changes in the T-wave. The heart muscle, owing to the myocardial lesion, may not contract normally, as far as we can judge by inspection, and yet the electrocardiogram may be normal. In one instance, however, a slight lesion did lead to changes in the T-wave, although the heart appeared to contract normally, but the microscopical examination of this heart revealed the presence of an unusual amount of scar tissue so that in reality the lesion was more extensive than it appeared to be. It seems that the more advanced the myocarditis the more one is apt to find a deviation of the T-wave from the upright position. In all our experimental animals the lesion was found in the base of the left ventricle and this location seems to be the cause of the T-wave alteration. We may conclude that the auricular myocarditis is not the cause of the T-wave changes, because in several rabbits the T-wave was inverted although no auricular lesion was found.

SUMMARY

1. Injection of caffeine and adrenalin causes a myocarditis in rabbits and we could show that this myocarditis causes changes in the electrocardiogram.

2. The main change in the electrocardiogram consists in an alteration of the T-wave.

3. The lesion in the base of the left ventricle is apparently the only myocardial change necessary to produce T-wave changes.

4. The auricular lesion produced experimentally by us suggests that amplification of the negative current produced in rabbits' hearts may perhaps show a change in the P-wave which was not observed in these experiments.

5. We believe that a continuation of this experimental study of myocarditis may throw light upon the exact nature of the T-wave.

6. Pericarditis does not cause an alteration of the electrocardiogram.

7. It does not appear likely that endocarditis causes a change in the electrocardiogram.

8. A small abscess in the myocardium does not influence the electrocardiogram.

REFERENCES

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THE RELATION OF OBESITY TO HEART DISEASE*

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THE relation of the obese state to disease of the heart is of considerable interest for two reasons: (1) Obesity often appears to influence the heart unfavorably, and (2) the explanations usually advanced as to why it does so are not convincing. Nevertheless, "fatty heart," so-called, has practically disappeared from recent medical literature. This is the more remarkable when one recalls that textbooks of medicine formerly contained important sections on fatty heart. In view of the above-mentioned facts the relation of obesity to the condition of the heart remains open for discussion. It is the purpose of this paper to review some of the facts pertaining to the subject and to offer a partial explanation, at least, of the manner in which the obese state influences the heart.

FATTY INFILTRATION AND FATTY DEGENERATION

Under the term "fatty heart" are embraced fatty infiltration and fatty degeneration. The essential features of the two conditions, as formerly described in a standard textbook of medicine, will bear repetition.

Fatty infiltration, according to Osler,[1] is usually a simple excess of the normal subpericardial fat. In pronounced instances the fat infiltrates the muscle, separating its fibers.

Fatty degeneration, so-called, is a common condition, and mild grades have been met with in many diseases. If the process is advanced the heart, especially the left ventricle, looks large and flabby.[1] The muscle has a light yellowish-brown tint, or, as it is called, a faded-leaf color. The splashes and streaks of fatty degeneration contrast with the normal areas, giving the variegated "tiger" or "tabby-cat" appearance. Microscopically, the fibers are seen to be occupied by minute globules distributed in rows. In advanced grades the fibers may appear to be completely occupied by the minute fat globules.

Even at the period from which the above descriptions have been taken we find such statements as "Fatty heart is no distinct pathological or clinical entity."[2] Pathologists have come to doubt the disease significance of fat in the heart. Delafield and Prudden[3] may be cited as asserting that small, or even considerable areas of fatty degeneration appear, as a rule, to be of little or no clinical significance; they are at least not inconsistent with perfect health.

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More recently a well-known internist writes: "In conclusion, it does not seem possible to establish a precise relation between the so-called fatty degeneration of the myocardium and failure of the heart. Moreover, we know that myocardial steatosis is only moderate in infectious myocarditis where the heart is obviously feeble but on the contrary is extensive in subacute phosphorus poisoning and in acute yellow atrophy of the liver where the cardiac symptoms are unimportant."[4]

In addition to the conditions noted above, Lusk[5] states that at autopsy large quantities of fat are found in the organs, especially the liver and muscles, in diabetes, anemia, arsenic poisoning, pernicious vomiting of pregnancy, eclampsia, cyclic vomiting in children, and after respiration of rarefied air (in an experimental chamber or at high altitudes above sea level).

A. M. Master[6] has reported the presence of fat globules, so-called fatty degeneration, in normal hearts; as for example, that of a healthy boy of eight years who was run over by a truck. It is well known, as stated above, that in pernicious anemia there is often a considerable degree of fatty infiltration in the heart. Nevertheless, no abnormalities were found in the electrocardiograms taken in a series of twenty cases of pernicious anemia.[7] It is, therefore, evident that fatty infiltration and degeneration are not limited to the heart and that they occur in many conditions besides obesity.

The writer has not available at the moment the percentage of cases of obesity that show a fatty condition of the heart (the literature abounds with the general statement that the association is frequent), and it does not seem essential to this discussion of the subject that such figures be obtained.

FAT FORMATION AND METAMORPHOSIS*

A large part of the body fat is derived directly from the fat moiety of the nutrition. Under normal conditions this is rebuilt chemically to accord with the characteristic fat of the species represented. Experiment has shown, however, that after fat starvation foreign fats may be temporarily stored as such in the body cells.

Fat may be formed by carbohydrate transformation. This probably implies a series of oxidation and reduction processes coupled with a conjugation of the simple hexose molecules.

As proteins have been demonstrated to be carbohydrate formers (see studies on diabetes and N-glucose ratios in the urine), they are potentially formers of fat. There is no specific evidence, however, to support this contention, as the conditions in which protein passes

*This section is largely a summary of the facts presented in Chemical Pathology, by H. G. Wells, ed. 5, 1925, W. B. Saunders Co., Philadelphia, pp. 445-449.

through a carbohydrate phase are usually diseases of a wasting character. The earlier concept of the transformation of protein to fat by degenerative changes has been proved untenable in the light of recent accurate chemical work. This statement deals only with the animal cell and not with bacteria or germinating seeds.

Many conditions of apparent fatty degeneration have been shown to be not degeneration but infiltration,—the fat appearing in seemingly larger quantity being derived from sources extraneous to those cells demonstrating an increased fat content. A striking illustration of the unreality of the increase in fat content is seen in certain liver conditions where the so-called fatty degenerated liver actually contains less fat than the normal organ. Redistribution and apportionment is regarded as the causative factor in the microscopic appearance of fat in such organs. Staining methods will not demonstrate this; chemical extracting procedures must be invoked. The explanation for this rests on the assumption that the lipoid content of the cell is frequently in such a state as to fail to respond to the common biological stains. It can be extracted and demonstrated, however, by chemical means, though here again the conjugation of the fats renders the simple ether extraction a nonquantitative procedure. Pathological changes may liberate this bound fat in such wise as to render it susceptible to staining and more freely extractable with ether. I believe that I am correct in saying that, without infiltration, organs seemingly grossly fatty in character contain never more than the normal amount and are usually below normal levels.

To summarize, then, the so-called "fatty degeneration" may result either from an infiltration of fat from external sources, due to degenerative processes going on within the organ, or through a reapportionment and chemical change in the fat content of an organ whereby microscopic evidences of fat masses are obtainable without any increase in the fat content of the organ. A third state is that in which both of these agencies operate. Circulating lipoids are probably the basis of the infiltration process, the necessary complement being injury to the cell whereby it becomes more permeable to fat. The other question of fat transformation depends upon chemical changes in the lipoids themselves whereby conjugate or combined substances are so modified as to produce larger percentages of simple fat at the expense of the conjugate fraction.

DISEASE SIGNIFICANCE OF OBESITY

Evidence has been given in the preceding paragraphs to show that fatty changes in the heart occur in conditions other than obesity. The deposition of fat from external sources into the cardiac fibers, and

the increased visibility of fat due to a physical alteration in the collodial state in which fat is prone to exist in the body, have been mentioned. It is believed that the reader will agree that fatty infiltration does not of itself harm the heart. In spite of this, it is true that the obese state is believed to be detrimental to the heart and especially so to those patients already affected by definite disease of the heart. Such belief finds support from the statistics pertaining to life insurance, chronic arterial hypertension and diabetes. Life insurance companies tell us that obese people do not live as long as others. Such individuals according to some statistics are more prone to be affected by high blood pressure; Foster[8] found that 50 per cent of his patients affected by chronic arterial hypertension were overweight. Parenthetically it may be stated here that size of the arm does not cause an inaccuracy in the determination of the blood pressure; for it has been demonstrated both clinically[9] and experimentally[10] that the resistance of the soft parts around the artery is a factor of no importance, provided the compressing armlet is at least 12 cm. wide, as is true of modern instruments.

Joslin has strongly emphasized the danger to the obese of developing diabetes.[11] This authority found 77.5 per cent of his patients were overweight and but 8.4 per cent underweight.* Also it has been found that diabetics are prone to early arteriosclerosis. Root and Warren,[12] in a study of the postmortem findings of twenty-six cases of diabetes, found arteriosclerosis in twenty cases and coronary sclerosis and myocarditis in eleven.

These structural changes found in diabetics are, of course, evidence of impairment of the heart. It is also well known that chronic arterial hypertension leads to cardiac hypertrophy and eventually to degenerative changes.

SOME EXPLANATIONS OF THE HARMFUL INFLUENCE OF OBESITY ON THE HEART

Considerations of space warrant the discussion of but three explanations, perhaps those more generally advocated.

1. The presence of fat in and about the heart in some way impedes the action of the organ. That this explanation is untenable must be evident from common clinical experience and the lack of relationship between the amount of fat present and the strength of the heart beat as summarized by Vaquez.[4]

2. Obesity adds extra pounds to the body and the carrying about of this excess weight increases the work of the heart. In my opinion

*These figures are averaged by me from Dr. Joslin's actual figures which were: 85 per cent of the Jewish patients were overweight, in contrast to 70 per cent of a mixed series of 1,000 Gentiles: 4.7 per cent of the former were underweight, in contrast to 12.2 per cent of the non-Jewish patients.

there is little truth in this conception of the detrimental effect of obesity on the heart. One cannot imagine any way in which the body could more readily transport a given number of pounds of baggage than if distributed as extra bodily tissue. And, furthermore, if there be anything in the effect of training in the ability to tolerate exercise it would seem that the body should become accustomed to the carrying about of the excess number of pounds, since it is always present and increases but slowly. The heart, like most other organs, has power enormously in excess of the usual demands made upon it. One must overlook this physiological attribute to hold that the heart is injured by the mere increase in the number of pounds of avoirdupois in an ordinary amount of obesity.

It also seems quite certain that the conception of the so-called "athlete's heart," i.e., one hypertrophied or damaged by increased physical exercise, is a myth.[13] For example, it has been found that the hearts of oarsmen,[14] of Marathon runners,[15] and of some six-day bicycle riders[16] were not enlarged.

The examination of the bicycle riders, immediately after dismounting from their ride, disclosed extraordinarily quiet heart action. The pulse rate did not exceed eighty in any, and in most it was in the sixties. The heart sounds were faint but the pulses were strong. Finally, I would like to quote from a recent study of the prevalence of heart disease among the clients of a large insurance company. The report states: "The incidence of circulatory disease is in inverse relation to the amount of physical exercise which the group takes in the open air and, other things being equal, it is in direct relation to the amount of nervous and mental strain."[17]

Exercise is known to be of value to the organism as a whole and to the heart also. In my opinion, it is only in cases in which organic heart disease (usually due to an infection) has caused a considerable reduction in the cardiac power that the excess number of pounds represented by the obesity can be considered of clinical significance purely from their mechanical effect of extra load.

3. There are more blood vessels (those in the fatty tissues) through which the blood must be pumped, thereby increasing the work of the heart. In its effect on the heart this explanation is merely a statement of another method by which the work of the heart is increased. It is subject, in my opinion, to much of the same objections as that given to the explanation based upon the extra number of pounds of body weight.

It is, furthermore, difficult to be impressed by the importance of the additional new blood vessels when we realize the vast number that exist normally. For instance, Krogh[18] is authority for the assertion that

the number of capillaries is enormous. In the muscle of a horse there are 1,350 capillaries in an area of but one square millimeter, while the corresponding figures for the dog are 2,630, and for the guinea pig 4,000. It was demonstrated, it is true, that under ordinary conditions blood flows through but a small number of this astounding array of blood vessels, but if the normal heart is devised to propel blood through such a huge stream-bed I find it hard to believe that the addition of some more vessels can do much harm.

In addition it should be remembered that it has been found[19] that the blood volume was actually diminished in patients who were obese. If the method of demonstrating the blood volume proves reliable, this reduction offers additional evidence against an increase in the work of the heart in obesity.

AUTHOR'S EXPLANATION

Since the explanations based upon a mechanical impediment to the heart or upon increased work of the heart do not satisfactorily account for the deleterious effect of obesity, it follows that something else must be the reason for the unfavorable influence of excess adipose tissue.

Some individuals, it seems, are apparently in good condition in spite of their obesity, but in general it may be said that the conditions that lead to obesity are not healthful. An ill balanced diet is generally considered the most common cause leading to the obese state. This diet is usually too rich in carbohydrate foods which, McCollum[20] believes, are today being used in excess by the average individual. The same authority also notes that this diet usually is lacking in vitamines and minerals, especially calcium. The importance of calcium has of late been freely discussed in medical literature.[21] Clark[22] (1916) has shown that digitoxin (the active principle of digitalis) is inactive without calcium. One sees occasional papers[23] wherein clinicians are taking this into account. Animals suffer in various ways when given diets inadequate in vitamine and in mineral content. Likewise, as has been emphasized by McCollum, human beings living on diets deficient in these elements suffer impaired health. If the skeletal muscles are not highly efficient when the diet is imperfect, is it not reasonable to assume that the heart muscle fares no better?

As perhaps a minor factor in the production of obesity is insufficient physical exercise. This error in hygiene naturally leads to a lack of physical fitness. Such a condition, of course, is hardly the ideal one for the heart. Physical exercise is now well known to be essential to the well-being of the heart and circulation.[24]

Doubtless enough has been mentioned above to indicate the writer's opinion that in the ill balanced diet and unhygienic manner of living found in most persons affected by obesity there is a partial explanation of the unfavorable influence of obesity upon the heart.

In addition certain statistical evidence has been presented that patients who are obese are prone to develop chronic arterial hypertension and diabetes, and either of these affections lead to arteriosclerotic changes in the organs of the circulation. It may well be that this arteriosclerosis is the cause of the more serious impairment of the heart in some cases of obesity. The exact mechanism by which arteriosclerotic changes arise cannot be said to be clearly understood; more light is needed on the subject. Aschoff,[25] however, has recently offered a convincing explanation of the origin of atherosclerosis. He finds that atheromatosis is due to the deposition of cholesterin esters in the connective tissue ground substance of the intima of the blood vessels. When these tissues become overloaded with lipoid substances, they become asphyxiated in the cholesterin esters, which then decompose into cholesterin and free fatty acids. These latter form soaps, the most important of which is that of calcium phosphate which is of bony hardness. Aschoff holds that the richness and character of the blood plasma is essentially influenced by the nature of the diet, and thus the occurrence of atheromatosis is favored. It is particularly after the age of thirty or more years that the atheromatous deposits are prone to change into definite atherosclerotic lesions. This is not the place to dilate further on the development of atherosclerosis; those interested are referred to Aschoff's article.

SUMMARY

Pathologists and clinicians alike have come to doubt the disease significance of fat in the heart.

Fat is present in the heart in many conditions besides obesity.

So-called "fatty degeneration" may be found in the normal heart.

A fatty condition of the heart may result from an infiltration from external sources, or through a reapportionment and chemical change in the fat content, whereby the fat already present becomes more visible, or both these agencies may operate.

Unless there is a deposition of fat from outside the heart the latter never has an increased content of fat; an increase may be apparent but has been proved not to be real.

"Fatty degeneration" is a misnomer; it does not result from the breaking down of the protein of the cells.

Fatty infiltration and "fatty degeneration" are now known to be but one process.

Nevertheless, from the clinical standpoint the obese state is considered to be detrimental to the heart.

Arterial hypertension, diabetes, and probably arteriosclerosis are more prevalent in obese persons.

The usual explanations of this unfavorable influence, based upon a mechanical impediment to the heart's activity or upon an increase in the work of the heart, are deemed unsatisfactory.

An excess content of fatty substances in the blood plasma has been shown to favor the development of atherosclerosis.

It is suggested that in the ill-balanced diet (i.e., one excessively rich in fat-producing foods, and deficient in vitamine and mineral content) and in the unhygienic manner of living, found in most persons who are overweight, there is a partial cause for the unfavorable influence of obesity upon the heart.

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Department of Clinical Reports

A DEPARTMENT OF CLINICAL REPORTS

WITH this issue of the AMERICAN HEART JOURNAL is begun a new department of Clinical Reports, designed for the recording of the details of unusual and interesting single cases.

The Editors and the Advisory Editorial Board believe that the publication of the records of carefully observed and accurately described cases, especially if these include postmortem findings, can be made to possess not merely an ephemeral interest but also a real and permanent value. It is within the experience of most physicians to encounter now and again some rare or unusually interesting case which is not sufficient in itself to form the basis of a formal article but which nevertheless deserves to be put on record.

It is only by the gradual accumulation of cases bearing certain resemblances to each other that the lineaments of disease entities and clinical syndromes sharpen and take form, and that nosological classification progresses.

In order, however, that such records may serve this useful purpose it is necessary that they comply with certain statistical requirements. Observations must be accurate and accurately described. Facts concerning the age of the patient; his previous state of health; the dates of the appearance of individual phenomena and their duration; the details of therapeutic procedures, when these are pertinent, should always be included. The evidence from which deductions are made should be presented fully. The facts should be made to speak for themselves.

Readers of the Journal are invited to cooperate in making the new department one of interest and value.

A CASE ILLUSTRATING THE LEUCOCYTOSIS OF PROGRESSIVE MYOCARDIAL NECROSIS FOLLOWING CORONARY ARTERY THROMBOSIS

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In attempting to recognize those cases presenting the clinical picture of "angina pectoris" that are due to thromboses in the distribution of the coronary arteries, attention is usually paid to the cardiac pain, the occurrence of nausea or vomiting* or both, fever, the presence of reactive pericarditis and certain electrocardiographic evidence. For many years we have laid stress upon other features of diagnostic value that may be present.[1] In cases of recent thrombosis these are, in brief, a sharp drop in blood pressure, marked diminution in the secretion of urine (or its suppression), leucocytosis, and the presence of old or recent thromboses elsewhere in the body. In those instances in which a clinical picture is suspected to be due to a thrombosis that occurred at an earlier time, we depend to a large extent upon the history, the presence of occluded arteries (especially in the lower extremities) and of aneurysm of the left ventricle, and a characteristic color of the face which is occasionally encountered.

As is well known, the diagnosis of even a recent thrombosis may be difficult. This is particularly true when the condition arises in a patient whom, according to a simple test, we may designate as hyposensitive.[2] In many cases the presence of leucocytosis may be of the greatest assistance. We have come to believe that no other finding is of greater diagnostic value. It is even safe to say that it is the most frequently significant feature of thrombosis of the coronary arteries. In the papers cited it is stated that the leucocytosis is usually due to myocardial infarction, but may also occur in connection with intracardiac thrombosis, even in the absence of any recent infarction. In one such case of intraventricular thrombosis, we found a leucocytosis as high as 24,200, with 82 per cent of polymorphonuclears.

The following case report is presented, as one of a number of similar experiences, to illustrate particularly another fact to which we have drawn attention, namely that when the leucocytosis does not disappear within a few days, it is necessary to keep in mind the possibility of

*Dizziness at times appears to be the equivalent of nausea and vomiting, in the hyposensitive, at least.

[1]Libman: Medical Record (New York), 1916, lxxxix, 124. Trans. Assn. Am. Phys., 1919, xxiv, 138. American Heart Journal, 1925, i, 121. Trans. Inter-State Postgraduate Assembly, Cleveland, Ohio, 1926. (In Press.)

[2]Libman: Trans. Assn. Am. Phys., 1926, xli, 305.

progressive necrosis of the heart muscle. Features of the case not directly relevant to the present theme will be discussed only briefly in this communication.

B. S., a man, married, aged fifty-three years was admitted to Mount Sinai Hospital, October 16, 1923, complaining particularly of severe pain "over the heart." There is a history of the presence of a "sore on the penis" many years previously. His wife has had one miscarriage. For four years there has been frequency of urination, twenty times daily and ten times at night. There has also been difficulty in starting the urinary stream.

According to the patient's story, cardiac symptoms were absent until six weeks before admission, when he began to develop dyspnea on slight exertion, palpitation and frequent attacks of precordial pain. On October 15th, thirty hours before admission, he was awakened by severe vise-like precordial pain, radiating to the entire left chest, left arm and leg, accompanied by profuse sweating on the left side of the body. The pain was severe enough to require the administration of morphine by hypodermatic injections. There was no loss of consciousness and no vomiting.

Physical Examination on Admission.—The patient is well nourished and well developed, acutely ill and in marked distress, dyspneic and cyanotic. The rectal temperature is 100.4°. The pupils are small but equal and regular, and react sluggishly to light and accommodation (central contraction by morphine). The fundi are negative. There is a band of hyperesthesia in the second and third left intercostal regions, anteriorly. The lungs show a boardy resonance throughout and coarse, bronchovesicular breathing. Numerous fine, moist râles are heard over both bases, posteriorly. There is a slight pulsation in the suprasternal notch, moderate retrosternal dullness and no sternal tenderness. The heart is enlarged, the action regular, and the rate 120 per minute. The heart sounds are distant and of poor quality and there are no endocardial murmurs. A loud to-and-fro friction rub is heard over the apex. The peripheral vessels are thickened but patent. The blood pressure is 135 systolic, 95 diastolic. The liver is felt 6 cm. below the free margin of the ribs, in the mammillary line. The spleen is not palpable. The arteries of the legs are patent.

Course.—October 17: According to the test that we employ, the patient is sensitive to pain. There is a soft, pericardial friction murmur in the region of the apex; the first heart sound cannot be heard, and the second heart sound is barely audible over the aortic area. The apex beat is weak. The radial pulses are small. There is marked tenderness in the left interscapular region. The liver dullness extends from the fourth rib to 4.5 cm. below the costal margin. The total length of the liver is 17.5 cm. in the mammillary line and 5.0 cm. in the midline. The entire free border of the liver is moderately tender. The left lobe of the liver extends 6 cm. from the spine, as determined by the Grocco method of percussion.

October 17.—At 10 P.M., (44 hours after the onset of the attack), the leucocyte count is 18,000 per cubic millimeter. The polymorphonuclear leucocytes are 84 per cent and the lymphocytes, 16 per cent. The erythrocyte count is 6,140,000, hemoglobin 120 per cent, and the color index 0.98 (consult table for leucocyte counts and temperatures). The Wassermann reaction of the blood is negative.

October 18.—The patient, being under the influence of a hypnotic, has slept most of the time. There is slight dyspnea, and cyanosis is evident. The heart sounds are almost inaudible. The friction rub is no longer heard. The blood pressure is 98 systolic, and 62 diastolic. The electrocardiogram, which on October 17 showed intraventricular block and no increase of auriculoventricular conduction time, now shows complete auriculoventricular heart-block, with atypical ventricular complexes.

Fig. 1.—Left side of heart, showing marked necrosis of the posterior wall of the left ventricle and adjacent portions of the interventricular septum and acutely developing aneurysm, consecutive to coronary thrombosis. Absence of extensive intraventricular thrombosis. Rupture of two of the pillars of the posterior papillary muscle. Hemorrhagic pericarditis. The probe indicates a perforation at the point at which the aneurysmal wall consists only of adhesions between the ventricle and the pericardium.

October 22.—The heart-block has disappeared. The pulse rate is 100, and the heart action is regular. The heart sounds are distant and feeble, and a faint pericardial friction rub is again heard over the apex. The blood pressure is 110 systolic, 85 diastolic. The apex beat is weak.

October 25.—There is dullness over both bases, diminished breath sounds and numerous fine, moist râles, especially on the left side. The patient complains of tightness over the precordium. The blood pressure is 90 systolic, and 70 diastolic. The liver measurement in the mammillary line is 22 cm. There has developed a pulsation between the apex beat and the sternum, marked enough to make one suspect that an aneurysm of the ventricle has developed, but not sufficient to warrant the diagnosis of that condition.

October 28.—The patient complains of pain in the left shoulder. There is fairly well marked tenderness on percussion in the left interscapular region. The heart sounds have continued to be almost inaudible. The pulmonary signs have become more conspicuous.

October 28, 8 P.M.—The patient has developed several attacks of severe, vise-like pain over the precordium, radiating to the left shoulder, together with anguish, and apprehension, a sensation of clutching at the throat, extreme weakness, dusky cyanosis of the nails and lips, and lividity of the skin. The pulse is very small and weak, the rate falling as low as 48 per minute. The rhythm is regular at times and coupled at other times. There are definite Head zones over almost the entire left chest.

October 29.—The general condition has improved, and there has been no further pain. The dyspnea, however, has increased. The apex beat is felt 11.5 cm. to the left of the midsternal line in the fifth interspace.

November 1.—At 8 P.M., the patient developed another attack of precordial pain, thoracic oppression and dyspnea, and the pericardial friction rub returned. The total length of the liver measures 17 cm. in the mammillary line.

November 3.—The patient died suddenly, today.

LEUCOCYTE COUNTS AND TEMPERATURES

DATE		WHITE BLOOD CELLS	POLYMORPHONUCLEAR LEUCOCYTES PER CENT	LYMPHOCYTES PER CENT	MONOCYTES PER CENT	TEMPERATURE (RECTAL)
10/16		18,000	84	16		100.4
10/17	A.M.	22,400	85	11	4	100.4
	P.M.	20,800	83	15	2	102.4
10/18		22,400	90	6	4	101.0-102.2
10/19		20,600	86	12	2	99.4-100.8
10/20		14,800	78	20	2	99.0-101.2
10/22		15,000	74*	23	3	98.6-100.6
10/23		13,500	80**	20		99.2- 99.8
10/25	A.M.	13,000	81**	16	3	99.4
	P.M.	15,400	74	22	4	100.8
10/26		18,600	80	18	2	99.0
10/27		18,800	78	20	2	99.2
10/28	A.M.	13,300	80†	16	4	98.8
	P.M.	20,100	72‡	26	2	99.8
10/29		19,800	78**	20	2	98.8- 99.0
10/30		13,600	73	26	1	99.0-100.0
11/1		10,000	79	21		98.8- 99.6
11/2		11,400	76	24		99.0- 99.2

*Including 1% basophiles.
**Including 1% eosinophiles.
†Including 2% eosinophiles.
‡Including 2% basophiles.

Temperature Curve.—See table.

Urine.—On October 16, 17, and 18 the amounts were 450, 406 and 650 c.c. respectively. From October 19 to October 24, inclusive, the amounts varied between 1100 and 1300 c.c. From October 25 until the death of the patient, the amounts varied from 550 to 900 c.c. Examination of the urine is negative.

Abstract of Necropsy.—(Performed by Dr. William Friedman.) The heart weighs 920 grams. The parietal pericardium is adherent to the anterior chest wall and the left lung by numerous tenuous fibrous adhesions. The two layers of the pericardium are bound to each other by recent and old adhesions, in the meshes of which there is found a thin layer of dark purple, clotted blood. The tricuspid and pulmonary valves are negative. The left auricle is somewhat dilated, its wall slightly thickened, and its endocardial lining whitened. The mitral orifice is of normal dimensions. There are several atherosclerotic patches on the aortic flap of the valve, and slight thickening of the edges of both flaps. Along the posterior border of the left ventricle, there is an oval-shaped aneurysm of the wall, extending to the angle between the ventricle and the septum, and involving the latter. The aneurysm occupies almost the whole length of the ventricle, its long diameter being 7.5 cm. and the transverse diameter being 4.4 cm. The wall of the aneurysm is thin, and the endocardial surface is denuded and shaggy in appearance, but there is only a slight deposition of thrombus. The muscle in the wall of the aneurysm is thin, and has an opaque, ochre appearance, indicative of recent necrosis. There is very little fibrous tissue in the muscular wall of the aneurysm. In searching for the site of the perforation of the aneurysm into the pericardial sac, no actual opening could be found, but the probe passed through at a point at which the aneurysmal wall consisted only of adhesions between the ventricle and the pericardium. This area is situated about midway between the apex and the base. The posterior papillary muscle is not included in the aneurysm, but is flattened and atrophic, and two of its muscular pillars, close to their attachment to the chordae tendineae, are ruptured. The anterior papillary muscle is essentially unaltered. The apex of the left ventricle is exceptionally thin, but is protected by a thick layer of edematous pericardial fat. The aortic valve is negative. The orifices of the right and left coronary arteries are patent. The circumflex branch of the right coronary artery, for a distance of about 3.75 cm. from its origin, shows marked atheromatous thickening and narrowing. Distal to this point, the vessel is occluded by a thrombus, for a distance of 4.5 cm. The posterior descending branch of the right circumflex artery is almost entirely occluded proximally by a thrombus, and distally by marked atheromatous changes. The short main trunk of the left coronary artery is patent, but the anterior descending branch is completely occluded by atheroma and an old, organized thrombus. Distal to the point of thrombosis, this vessel is almost completely obliterated by atheroma alone. The left circumflex branch is a narrow cord of small caliber, and is completely occluded 0.5 cm. from its point of origin. This vessel can be traced to the margo obtusus, and gives off a descending branch which is markedly thickened and narrow, and is practically occluded by an old thrombus at a point 3 cm. from its origin.

The lungs show congestion and edema, but no pneumonia or infarction.

The liver, spleen, kidneys and gastrointestinal tract show marked passive congestion.

COMMENT

Briefly summarized, the case is one of a man fifty-three years of age, the story of whose past history is not altogether reliable, who suddenly developed an attack of severe precordial pain radiating to

the left shoulder and arm, which was followed by dyspnea, cyanosis, Head zones in front and back, fever, pericarditis and conspicuous polymorphonuclear leucocytosis. He died after an illness of eighteen days, during which period the leucocytosis, slight fever and thoracic hyperesthesia persisted, and the physical signs led to the suspicion of the development of an acute aneurysm of the heart. The chief interest centers about the white blood counts, the first of which was made forty-four hours after the onset of the attack. It revealed a leucocytosis which persisted in varying degree until the death of the patient. Causes for leucocytosis outside the heart, in particular, pulmonary inflammation or infarction,* were searched for, but were not found. Infarction of the myocardium, consecutive to coronary thrombosis, was proved by the postmortem examination to be the sole cause of the leucocytosis.

The leucocytosis accompanying infarction of the myocardium may develop as early as one hour and fifteen minutes after the onset of the symptoms. The counts in our cases have varied between 9200 with 81 per cent, and 25,500 with 83 per cent polymorphonuclear leucocytes. The lowest percentage of polymorphonuclear leucocytes found was 78, and the highest 91. In more than one-half the cases, the white blood cell counts ranged between 15,000 and 20,000.

As the leucocytosis in the present case did not recede within a few days, the presence of progressive necrosis of the heart muscle was suspected. A perusal of the table indicates clearly how much more valuable the leucocyte counts may be than the degree of fever, in judging the condition of the patient. This experience is not at all an infrequent one. Not only is it important to make the leucocyte counts for the purpose of diagnosis, but also for prognosis and management.

Other points in favor of progressive myocardial necrosis were the persistent slight but definite febrile reaction, the recurring pericardial friction rub, the persistent tenderness in the back, and the development, on the eleventh day, of a new pulsation between the apex and the left border of the sternum. In a number of cases of aneurysm of the anterior wall, which we have been able to recognize clinically, we have found that it is often characteristic to encounter the association of a feeble or absent first apical sound and a pulsation which is most marked between the apex of the heart and the sternum, and which is more forcible than would be expected from the intensity of the heart sounds. In the case which we are reporting, the evidence was not, to our minds, sufficient to venture a positive diagnosis of aneurysm. It is of interest to note, however, that suggestive signs

*Hemorrhagic infarction of the lungs may cause conspicuous leucocytosis, the count in one of our cases, being 34,000 with 97 per cent polymorphonuclear leucocytes.

were present, despite the fact that the aneurysm had developed in the posterior wall of the left ventricle.

There were no signs during life which pointed to the rupture of a papillary muscle. At times, clinical evidence of this condition presents itself. Inasmuch as the posterior papillary muscle of the left ventricle receives its blood supply from the posterior descending branches of both coronary arteries, when the distribution of the latter is typical, it is necessary that both these branches be occluded before this papillary muscle may be sufficiently damaged to rupture, a fact which is illustrated in our case.

A CASE OF RECURRENT BENIGN FIBRINOUS PERICARDITIS

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WHILE occasionally an individual is seen suffering from recurrent attacks of a dry pleuritis, we are unaccustomed to meet the corresponding condition occurring repeatedly in the pericardium. Yet, I have had the opportunity of observing a patient for over three years, during which time he has had seven attacks of undoubted pericarditis, of short duration, afebrile in character and of unknown etiology.

A search of the literature has failed to reveal mention of a similar condition and the standard text and reference books do not speak of it.

Mr. F. W., aged 36 years, was first taken ill on September 24, 1923, with a sharp, sticking pain above the ensiform cartilage. The pain gradually increased in intensity, and six hours after the onset I was called to see him.

The patient gave the following history: He had had measles in childhood, but had never had tonsillitis, chorea, rheumatism, scarlet fever or typhoid fever. He had never had a chest injury. He had never contracted a venereal infection. He was a very moderate user of alcohol and tobacco. In 1918, he had cholera nostras in a very severe form. In February, 1923, he had a sore throat which lasted three days. He had no joint involvement and no cardiac symptoms at that time. His attack, as noted above, began six hours before I saw him, with a sharp, sticking pain just above the ensiform cartilage, radiating to the left toward the region of the nipple. He had been well before the onset of pain; had had no dyspnea or palpitation on exertion and had never had precordial distress while walking. There was no history of cough, nosebleed or joint pains. The patient stated that the pain in the chest became aggravated on leaning forward and when he turned on his left side. His bowels had been constipated, and he had noticed some belching after meals. He had never had abdominal pain. There had been no nausea or vomiting.

On examination, the patient appeared to be having a good deal of pain, but did not seem acutely ill. His rectal temperature was 99°, his respiratory rate 14, and his pulse, which was regular and of good force, was 76. He was a tall, thin man, with a markedly sallow complexion, coated tongue and heavy breath. His tonsils were enlarged and diseased. The teeth were in good condition. None of the superficial lymph nodes was enlarged. The chest was flat. The lungs were entirely clear. The heart was not enlarged to percussion. There were no visible pulsations over the cardiac area and no thrills could be felt either at the apex or over the base of the heart. Just above the ensiform cartilage could be felt a soft, creaking, to and fro rub. The sounds were regular, slow and of good quality. No murmurs were heard over any of the valve areas. Heard just above the ensiform cartilage and in a rectangle, extending from the ensiform to the left for a distance of 5 cm. and upward for a distance of 3 cm., there was a soft, swishing, to and fro friction murmur. This was accentuated by making the patient lean forward and also by turning him 45° to the left. These motions accentuated the pain. The murmur was also heard posteriorly a little to the right of the angle of the left scapula. It was in no way

affected by respiration,—either by making the patient breathe deeply or by having him hold his breath. The sternum was not tender to percussion. The abdomen was flat, with no areas of tenderness and no enlargement of the liver or spleen. A superficial neurological survey showed no abnormality of the reflexes. There was no pretibial edema. Rectal examination revealed a few external hemorrhoids. The genitals were normal.

The patient received small doses of codeine to control the pain and daily colonic irrigations. In twenty-four hours, the friction rub had lessened in intensity and no new findings had come to light. The temperature did not rise above 99.2°. In seventy-two hours, the friction murmur had entirely disappeared, and over the area where it had been heard the skin was peculiarly sensitive to touch notwithstanding the fact that no ice bag or counterirritant had been used. The pulse rate never rose above 80 during this period and the respiratory rate remained normal. After the attack had apparently subsided, the patient complained of extreme weakness. On this account, he was kept in bed for two weeks, but during this time there was no recurrence of the pain or the friction rub. A blood examination, made while the friction murmur was heard, showed the following:

Hemoglobin	72%
Red blood cells	4,100,000
White blood cells	8,000
Differential	
Polymorphonuclear leucocytes	71%
Small lymphocytes	24%
Monocytes	4%
Eosinophiles	1%

After the patient had regained some strength, it was determined to search for all possible foci of infection. Thinking that perhaps the lesion in the pericardium was tuberculous in nature, fluoroscopy was done and x-ray films of the chest were made. The lungs were entirely clear. The heart showed no enlargement, and no evidence of enlarged mediastinal lymph nodes was found. X-ray examinations of the accessory nasal sinuses showed them to be clear. Electrocardiographic examination gave evidence only of slight left ventricular preponderance, but no other abnormality. X-ray films of the teeth showed no periapical abscesses and no devitalized teeth. The tonsils were thoroughly examined and found to be diseased. Subsequently, they were removed. Chemical examination of the blood showed the following:

Urea nitrogen	19.2 mg. per 100 c.c.
Incoagulable nitrogen	36.8 mg. per 100 c.c.
Creatinin	1.1 mg. per 100 c.c.
Uric acid	2.5 mg. per 100 c.c.
Sugar	0.092%
Cholesterin	186 mg. per 100 c.c.

The urine was acid, had a specific gravity of 1018, showed no albumin or sugar and was negative on microscopical examination. The Wassermann test of the blood was negative. Massage of the prostate yielded no pus cells.

Aside from the diseased tonsils, these efforts yielded little return in the way of uncovering an etiological factor for this peculiar attack. After the tonsils were removed, the patient was placed on a low protein diet, his intestinal tract kept clear

by frequent colon irrigations and he was allowed to return to his business. He continued to complain of weakness and extreme exhaustibility. Thyroid extract did not improve this condition, but he had no cardiac complaints and no recurrence of the pain. He remained in this condition until February 10, 1924, when he again had an attack of sharp pain localized above the ensiform, and a repetition of the same findings as in the first attack. The friction murmur was again heard in the same area, but this attack was much milder than the first one. The rub disappeared in forty-eight hours and left the same skin sensitivity. Blood examination again failed to show a leucocytosis, and there was no elevation of temperature during the attack. As in the original attack, the patient developed no lung signs and no manifestations of rheumatic fever. In four days, he was quite well, the pain having entirely disappeared and he was able to return to his business. He still complained, however, of extreme exhaustibility.

A third attack occurred in June, 1924, entirely similar to the first two. At this juncture, the patient felt that little headway was being made in discovering the etiology of these attacks, and determined to be reinvestigated. This was done by other observers and the results already obtained were confirmed. In addition, the gall bladder was drained by the Lyons' method, but no focus of infection was found. X-ray examination of the entire gastrointestinal tract was negative. His basal metabolism was normal and his blood showed no changes. Thus far nothing positive had been determined to explain the onset of these peculiar attacks of chest pain, accompanied by the soft, swishing friction murmur, heard over the lower cardiac area.

Mild attacks occurred in January and June, 1925. In July, 1925, another series of investigations again resulted in entirely negative findings.

In September, 1926, a sixth attack occurred. In this attack, the pain was somewhat more severe and the friction rub louder, but in all other ways the attack was similar to the others. The absence of temperature, pulmonary signs or joint manifestations made us feel that these attacks were probably due to some metabolic disorder. It was determined to give the patient a series of intestinal colon bacillus implantations, with a view to affecting the intestinal flora. It had been observed that in gouty individuals this treatment seemed to lessen both the frequency and intensity of the attacks, although not entirely eliminating them. At the conclusion of the treatment, he reported that he felt better than he had in years. He felt fresh, his exhaustibility had left him, and he had gained eight pounds in one month. Despite this improvement in his general condition, he had a sharp attack on December 28, 1926, just two weeks after he had concluded his treatment. Wishing to obtain some fresh laboratory determinations during an attack, I had him removed to Mount Sinai Hospital. The attack lasted forty-eight hours and the nature and position of the friction rub were unchanged. The temperature ran between 98.8° and 99.2° (rectal) for the two days. The pulse rate was never accelerated. After the first twelve hours, he developed showers of fine subcrepitant râles at the bases of both lungs—a physical sign he had never had on previous occasions. These râles disappeared with the friction rub. The pharynx was decidedly reddened. His blood examination during this attack showed the following:

First 24 hours:

White blood cells—10,000

Polymorphonuclear leucocytes	81%
Small lymphocytes	18%
Eosinophiles	1%

Second 24 hours:

White blood cells—8,000	
Polymorphonuclear leucocytes	73%
Small lymphocytes	26%
Eosinophiles	1%

Blood chemistry:

Urea nitrogen	18.2 mg. per 100 c.c.
Incoagulable nitrogen	33.4 mg. per 100 c.c.
Creatinin	1.2 mg. per 100 c.c.
Sugar	0.095%
Cholesterin	178 mg. per 100 c.c.

X-ray and fluoroscopy of the chest revealed nothing abnormal. It was particularly interesting to note that, despite the frequency of these attacks, there were no demonstrable adhesions between the visceral pericardium and the diaphragm, and that the heart was not enlarged. Similarly, the electrocardiogram gave no evidence of any abnormality.

The recurrence of the symptoms and signs, at a time when the patient stated that he was in better health than he had enjoyed for some years, makes it doubtful if any metabolic factor alone can be playing the entire rôle in inducing the roughening of the pericardium. While it may not play a large part in the picture, the appearance of the pulmonary signs and the inflamed throat make me believe that there is some infectious agent necessary to induce an attack. Perhaps this agent is of the nature of the virus of rheumatic fever. I feel that there will probably be future attacks, in one of which the causative factor may show itself.

LOCAL SCLEROSIS (HEALED INFARCT) OF THE HEART IN AN INFANT*

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A COLORED female infant, M. H., nineteen months of age was admitted to the pediatric service of the Cincinnati General Hospital on November 24, 1924. The chief complaint was a dry paroxysmal cough which had been gradually increasing in severity over a period of four weeks. Fever and other symptoms had been absent and the child had not seemed ill until a few days before admission. On the initial examination the rectal temperature was 101° F., the pulse rate varied between 130 and 140 and the respirations between 55 and 60. Considerable dyspnea and a frequent dry cough were present. Physical examination revealed the following deviations from the normal: (1) Slight puffiness around the eyes, without evidence of edema elsewhere; (2) purulent nasal and postnasal discharge and injection of the throat and tonsils; (3) an inflamed and bulging tympanic membrane in the right ear; (4) an enlarged liver extending about 6 cm. below the costal margin in the midclavicular line, and a spleen 4 cm. below the costal margin; (5) limitation of motion, impairment of resonance, distant and suggestively tubular breathing and some medium-sized moist râles in the left axilla and over the base of the left lung as high as the angle of the scapula—the right lung showing harsh and exaggerated breathing and diffuse rhonchial sounds and medium-sized moist râles; (6) a rapidly acting heart showing definite gallop rhythm, with a right border the percussion dullness of which was apparently in the normal position and a left border which merged into the area of axillary impairment already noted. There was no clubbing of the fingers. The child's dark skin made the determination of cyanosis difficult, although the color of the nail beds and the mucous membranes suggested its presence.

The patient had been born prematurely at seven months after an easy labor. The birth weight was unknown. Breast feeding was continued until the child was about nine months old. Development was slow and the weight at one year was only 15 pounds. At eight months of age acute otitis media developed and after a spontaneous rupture of the tympanum, drainage continued for about a month. At ten months of age an uneventful attack of varicella occurred, but there had been no other acute illness or febrile attack of any nature until the acute otitis media at the time of the first admission to the hospital. From time to time since the age of two weeks there had been a rather mild cough. There was nothing in the history which suggested the occurrence of clinical signs of syphilis. The mother had had one miscarriage before the birth of the patient and at the time of admission of the child was again pregnant. There had been no known exposure to tuberculosis.

Paracentesis of the right tympanic membrane resulted in a fall of temperature to normal and an improvement in the patient's condition, but the rapid pulse and respiratory rate continued. The history and the physical examination on admission were such that the diagnosis of pneumonia was made. The possibility of fluid at the left base was considered, but the lack of cardiac displacement to the right and the absence of signs indicating compression of the upper part of the left lung suggested that this, if present, was small in amount. A roentgenogram taken the day after

*From the B. K. Rachford Department of Pediatrics, University of Cincinnati.
Read before the American Pediatric Society, June 2, 1926.

admission showed marked cloudiness at the left base continuous with the heart outline and this was interpreted as being due to pneumonic consolidation.

The patient was removed from the hospital after several days and readmitted on January 2, 1925, when twenty-one months of age. In the interval she had continued to cough but the father stated that he had not thought that she was sick and only brought her for observation at the request of a visiting nurse. Her temperature was 99°, the pulse rate 135 and the respiration 56. The weight was 19 pounds. With the exception of the fact that the otitis was no longer present, the physical examination at this time was similar to that noted at the previous admission.

Roentgen-ray and fluoroscopic examinations of the chest disclosed a very large heart filling the entire left lower chest and the fact that the impaired resonance and other physical findings in this region were due to the heart and not to pneumonia or fluid. A picture taken in the lateral position demonstrated that the base of the lung was clear. Urine examination revealed nothing abnormal. The red blood cells were about 5,000,000 and the hemoglobin 65 per cent (Tallquist). The white blood cells counted on several occasions varied from 8,000 to 10,000 and the polymorphonuclears from 44 to 66 per cent. Intracutaneous human and bovine tuberculin tests were negative. Sputum obtained by swab from the throat was negative for tubercle bacilli. The blood Wassermann test was negative. The blood pressure was about 90 to 95 systolic and 60 to 65 diastolic.

During the next few weeks the patient's condition remained unchanged. The temperature continued normal or subnormal, respirations were rapid and there was definite dyspnea. The gallop rhythm of the heart subsided but the action continued rapid (130 to 140) and was forceful. Pulsation could be felt as far to the left as the midaxillary line, 7 cm. to the left of the midsternum. Impairment of percussion could be made out not only over this region but it continued to be present at the left base. The pulmonic second sound was relatively louder than might be expected at the patient's age. A short, soft, somewhat blowing systolic murmur which did not entirely replace an impure first sound developed near the apex. About a month after admission the temperature became elevated, numerous moist râles developed throughout both lungs, gallop rhythm returned and the heart action and sounds became gradually and increasingly feeble. Death occurred on February 19, 1925, when the patient was about twenty-three months of age. The clinical diagnosis was idiopathic cardiac hypertrophy with dilatation and myocarditis.

Necropsy was performed by Dr. J. Ganim of the Department of Pathology. The pericardial lining was moist, smooth and glistening and the sac contained 10 c.c. of clear yellow fluid. The heart was enlarged, especially in the region of the left ventricle and weighed 135 gm. The ductus arteriosus and the foramen ovale were closed and the pulmonary artery was patent and not hypoplastic. The endocardial linings were smooth and both auricular and ventricular septa were intact. The valve leaflets were smooth except for barely perceptible thickening on the free border of one of the mitral segments. The diameter of the tricuspid opening was 53 mm., of the mitral 55 mm., of the aortic 42 mm., of the pulmonary 40 mm. The papillary muscles appeared hypertrophied. A large part of the left ventricular wall was hypertrophied but in the region of the apex there was a sharply circumscribed area about 3 cm. in diameter consisting of firm, white scar tissue which extended through the entire myocardium and which was much thinner than the surrounding muscular wall. Scattered throughout the myocardium in the immediate region of this scar were irregular smaller scarred areas (See Fig. 1). The greatest thickness of the left ventricular wall was 12 mm. and of the right ventricular wall 3 mm. The coronary vessels and the aorta throughout their entire length possessed smooth, pale, glistening linings. The thymus appeared normal and weighed 10 gm. There was no free

fluid in the pleural cavities. The lungs showed some small areas of atelectasis, considerable fluid in the bronchial tubes but no pneumonic consolidation. The liver and spleen were enlarged and congested, the spleen weighing 20 gm. The gastro-intestinal tract showed no gross pathological change. The pancreas, adrenals, ovaries, uterus and tubes were normal in size and appearance. The kidneys each weighed about 45 gm. Their external surfaces were smooth except for some small gray pitted areas, none of which exceeded 0.5 cm. in diameter. These were discrete and four of them were found in each kidney. On section they were found to have a triangular outline with the base at the periphery and to extend only a short distance into the cortex. Otherwise the kidneys showed nothing abnormal but congestion.

Fig. 1.—The left ventricular wall is split open showing the scar tissue which involves the region of the apex throughout the entire thickness.

The microscopical examination of the heart showed moderate congestion and variation in size and vacuolation of the muscular fibres and, in the sclerosed areas, extensive fibrous tissue replacement in various stages. The kidneys showed venous and capillary congestion, edema of all renal elements and in the small triangular areas noted on gross examination there was increased connective tissue with sclerosis of the included glomeruli. In none of the other organs such as the thymus, liver, spleen, pancreas and adrenals was any notable change demonstrated except congestion and edema. In the lungs there were patches of endothelial leucocytes in the alveoli, edema of the interstitial tissue, endothelial proliferation of lymphoid tissue along the bronchi and patches of atelectasis. The *anatomical diagnoses* were: cardiac hypertrophy and dilatation; chronic fibrous myocarditis (healed infarct in the wall of the left ventricle); multiple healed infarcts of the kidneys, and acute bronchitis.

COMMENT

This case is instructive for several reasons. In the first place the physical and roentgen-ray findings suggested the diagnosis of pneumonia of the base of the left lung or of fluid in the left pleural cavity. The continuation of the signs and the absence of fever and leucocytosis after the otitis had improved caused the search for another cause which would explain the symptoms. The confirmation of the diagnosis of an enlarged heart was greatly aided by the fluoroscope as well as by roentgen-ray pictures. It was then easy to account for impaired resonance and the like at the base of the left lung by the compression of that organ by the enlarged heart. The age of the patient and the character of the murmur, when this was present, were against the probability of acquired heart disease although we know that this may occur in rare instances in infants under two years of age.* To be considered, of course, in the clinical diagnosis was the possibility of congenital heart disease. The absence of clubbing of the fingers and of marked cyanosis, the lack of demonstrable enlargement of the right side of the heart and of cardiac thrill and rough murmur pointed to the fact that none of the usual types of congenital cardiac lesion was present. Congenital idiopathic hypertrophy of the heart, therefore, seemed a reasonable consideration. It was only necropsy which could discover the actual cardiac lesion present in this case.

It is interesting to speculate upon the cause of the original damage to the heart which resulted in the formation of the area of scar tissue. It was apparently in the nature of an infarct involving one of the branches of the coronary artery. This, taken in conjunction with the infarcts in the kidney, which were of the same age, would indicate that the patient had at one time suffered from a general infection of a septicemic nature. An acute otitis media at eight months of age and chickenpox at ten months were the only infections which the patient had had previous to her admission to the hospital. It has been our experience to see severe complications following chickenpox. These have sometimes been of such a type (myelitis and encephalitis, for example) as to denote a general blood stream invasion by the causative virus or organism. The predilection is not always for nervous tissue, and pneumonia and empyema also occur frequently enough and at a time to indicate a connection between these conditions and chickenpox. In this case the otitis media, presumably occurring as part of an acute upper respiratory infection, probably constituted the starting point for the septicemia.

The sclerosed lesion found in the heart of our patient resembled that found in adults connected with disease of the coronary arteries and

*Denzer, B. S.: Jour. Amer. Med. Assn., 1924, lxxxii, 1243.

the location is one of the most common in such a condition. An angiosclerotic process could hardly occur in an infant, especially in the absence of syphilis.

The weight of the heart was that of a normal child of eleven or twelve years of age and at least twice as great as the normal heart at two years. The thicknesses of both left and right ventricular walls were only slightly less than those of an adult heart. The diameters of the valves were approximately half those of the adult heart.

Department of Reviews and Abstracts

Selected Abstracts

Clerc, A., and Levy, R.: Concerning the Electrical Tracings of Myocardial Insufficiency. Compt. rend. Soc. d. biol., 1926, xciv, 759.

This brief paper is devoted to a discussion of so-called "arborization block," originally reported in this country by Oppenheimer and Rothschild. The authors believe that the characteristic electrocardiograms are not necessarily due to changes in the terminal ramifications of the Purkinje system, but rather to fatigue of the cardiac musculature and the difficulty which the wave of excitation encounters because of successive barriers in conduction fibers structurally or functionally modified. The prognosis is grave, for of nineteen patients exhibiting the typical curves, sixteen died, the majority a few weeks after the tracings were made. Of the remaining three patients, one left the hospital in bad condition and the other two were in the hospital at the time the paper was written.

Williams, H. B., and Dodge, H. F.: Analysis of Heart Sounds. Arch. Int. Med., 1926, xxxviii, 685.

Studies have been made of the frequency distribution of the energy of normal heart sounds as heard at the apex of ten male adults. The apparatus used for this purpose consisted of the electrical stethoscope and a special electrical frequency analyzer which made it possible to determine the relative amounts of energy in the different frequency components of the complex electrical waves. This work has been restricted to a study of the energy above 50 cycles. Indications of later work point out that there is a considerable amount of energy below this point, although data were obtained for frequency up to 300 cycles. Such a small percentage of the energy lies in 10 cycle bands above 150 cycles that it is not possible to show in the charts.

The relative amounts of the higher frequency energy vary considerably in the ten persons. The authors found that in the cases in which the heart sounds were richest in high frequency components there was 1/10 the amount of energy in the band 90 to 100 cycles compared with the energy between 50 and 60 cycles, and in the band 190 to 200 cycles about 1/1000 of that energy. In the other extreme case in which the sounds were poorest in high frequency components the amount of energy in the band 90 to 100 cycles was 1/1000 of the energy in the 50 to 60 cycle band and between 190 to 200 cycles approximately 1/100,000 of that energy. This variation in the distribution of the vibrational energy is what determines the characteristic quality of the heart sounds of different persons.

Aside from the consideration of quality, it was noted that for thin chested persons more energy was available at the sternum than at the apex, while for those of more solid construction the energy usually was greatest at the apex. In several cases there was no marked difference in the energy in these two areas. For purposes of study about twenty male adults were chosen at random without thought of having cases of extremely loud or extremely weak heart sounds. For each the area

of maximum sound intensity was selected and by suitable electrical measuring apparatus the sound energy at this point was determined. In this study a ratio of over 40 to 1 in sound energy was observed between the loudest and weakest normal heart sounds for the persons in the group.

The authors also studied the frequency composition of fetal heart sounds as compared to that of normal heart sounds. For fetal sounds the amount of sound energy is considerably smaller; the ear must operate close to the threshold of audibility. Acuity of hearing the low frequency is obviously an essential requirement in obstetrical auscultation. By the same general method the frequency components of low pitched and high pitched heart murmurs have been studied. Charts are produced in the article showing the distribution bands of these murmurs. The first chart shows that for 11 low pitched murmurs there were always components of sounds in the band 120 to 400 cycles per second and in 9 out of 11 there were components up to 120 cycles per second. Broadly speaking, the low pitched murmurs cover a range up to 400 cycles per second. The second chart shows that for 22 murmurs described as moderately high or high pitched, there were always components of sound within the band 240 to 400 cycles per second and 19 with over 22 components within the band 240 to 600 cycles per second. From this the band 120 to 660 cycles can be considered of greatest general importance for these high pitched murmurs.

Pichon, E., and Larde, Arthes, C. R.: Concerning a Case of Progressive Cardiac Rheumatism with Multiple Pulmonary Infarcts and Specific Nodular Myocarditis. Arch. d. Med. des Enfants, 1926, xxix, 581.

The authors report a case of progressive cardiac rheumatism (see AM. HEART JOUR., 1925-26, i, 382) in a child of five years, lasting for seven months. The autopsy revealed serofibrinous pericarditis, cardiac hypertrophy and dilatation, mitral stenosis and insufficiency, aortic insufficiency, fresh vegetations on the mitral and aortic valves, multiple small infarcts in both lungs and chronic passive congestion of the viscera. Aschoff bodies were found in the myocardium and in the aortic and mitral valves. Inasmuch as there were no thrombi in any of the pulmonary vessels, the authors interpret the infarcts as multiple foci of "pulmonary apoplexy," i.e., hemorrhagic extravasations from ruptured small pulmonary veins resulting from passive hypertension in the pulmonary circuit of mitral origin.

Branch, Arnold, and Linder, Geoffry C.: The Association of Generalized Arteriolar Sclerosis with High Blood Pressure and Cardiac Hypertrophy in Chronic Nephritis. Jour. Clin. Inves., 1926, iii, 299.

In the present paper the authors report observations on the microscopical examination of the vessels of the kidney and other organs in ten consecutive cases of chronic nephritis in young patients coming to autopsy after previous clinical observation and functional study for some time in the hospital. The data may assist in the eventual clarification of the relationships of renal function and blood pressure changes to cardiac and vascular alterations.

Three cases died of intercurrent infections. These cases showed relatively mild but definite, diffusely distributed glomerular lesions. They were free from hypertension, arteriolar sclerosis or cardiac hypertrophy and demonstrate that glomerulonephritis can develop to a considerable degree without such results.

Seven cases came to typical nephritic death; six in uremia and one from heart failure. All of these cases showed hypertension and neuroretinitis together with cardiac enlargement, gross in five cases, moderate but probably definite in two. These findings are in accord with the current view that cardiac enlargement in nephritis is the result of hypertension.

In six of these seven cases arteriolar sclerosis of the parenchymatous organs was found at autopsy. The concurrence of the arteriolar sclerosis so frequently with retinitis and hypertension shows that the presence of hypertension in nephritis indicates usually but not always a coexisting arteriolar sclerosis.

One nonconforming case shows that arteriolar sclerosis may be absent if the neuroretinitis and hypertension have existed for several months accompanied by renal insufficiency advancing to uremia.

Clawson, B. J.: Experimental Rheumatoid Myocarditis. Arch. Path. and Lab. Med., 1926, ii, 799.

In cultivating blood taken from patients having acute rheumatic fever, streptococci, usually viridan strains, were commonly found. The organisms when first seen in the liquid medium were regularly observed to be in clumps, as if agglutinated. It was suggested that the Aschoff nodule might develop as a result of clumps of agglutinated streptococci lodged in the small vessels of the heart. Thirty-four rabbits were inoculated intracardially with about 5 c.c. of a suspension of agglutinated streptococci and were given each from one to eight injections. Animals were killed or died at intervals of from one to sixty days after the first injection. Myocarditis to some extent occurred in all but one, as shown in the accompanying table. The most constant reaction was proliferative in character, being present in all but one of the thirty-four animals.

These experiments show that experimental myocarditis and pericarditis are regularly produced in rabbits by injecting agglutinated streptococci. As in human rheumatic myocarditis, the inflammation is located chiefly in the interstitial structures around the blood vessels and in the subendothelial structures. The similarity of microscopical appearance of human rheumatic and experimental rabbit carditis is pronounced. The inflammation is chiefly proliferative. The exudate is largely mononuclear cells such as macrophages, plasma cells and lymphocytes. The presence of multinucleated cells with vesicular nuclei is characteristic in both cases. The staining reaction of the macrophages and multinucleated cells to methyl-green-pyranin is similar in both human rheumatic and experimental myocarditis. The great frequency of nodular proliferative inflammatory areas with mononuclear and multinucleated cells in the experimental myocarditis suggests a similarity to human rheumatic myocarditis.

Small, James Craig: The Bacterium Causing Rheumatic Fever and a Preliminary Account of the Therapeutic Action of Its Specific Antiserum. Am. Jour. Med. Sci., 1927, clxxiii, 101.

The author presents in this report the description of a streptococcus which has a specific immunological identity; which he has isolated in the first instance from the blood of a patient suffering from rheumatic fever; which he has cultured in each instance from the throats of patients with rheumatic fever. This streptococcus is capable of producing characteristic arthritic and cardiac pathology, including Aschoff nodules. A specific therapeutic serum has been prepared which is effective in terminating the toxemia and other clinical manifestations in the patient suffering from acute rheumatic fever. For this organism the name "Streptococcus cardio-arthritides" is suggested.

The organism was isolated from a blood culture made on April 5, 1926 on a patient, C. L., medical ward 335, Philadelphia General Hospital. Culture was made in infusion broth and showed growth turbidity on the ninth day of incubation. Smears show a gram-positive coccus in short chain formation. Subculture upon the

surface of horse blood agar showed small gray colonies producing absolutely no change upon the medium. Blood serum obtained from the patient ten days later agglutinated the strain in dilutions up to 1:320. The organism was then inoculated into rabbits resulting in various changes resembling rheumatic fever. These biological and morphological changes are described in detail in the protocols. Nine patients suffering from rheumatic fever were then treated by means of an antiserum prepared from a strain of streptococcus isolated from the blood of a patient with rheumatic fever. Two of the patients chosen showed later that the correct diagnosis was other than rheumatic fever. In these no improvement followed the use of the serum. In all the remaining patients a very prompt improvement followed the injection of the serum in sufficient dosage.

When this organism is inoculated into rabbits, it has been shown to produce acute arthritis comparable to that of rheumatic fever in humans and a proliferative osteoarthritis comparable to a type of chronic arthritis in humans. The acute illness in rabbits is attended by marked tenderness, redness and swelling of the joints involved, by profound asthenia and atrophy of the skeletal muscles, by central nervous system involvement producing extreme excitability of the animals and pronounced choreiform movements, nodding spasm and flaccidity of one or more of the legs. The infection appears to persist in subacute and chronic stages when animals survive the acute attack of the disease.

Further work will be awaited with great interest. Control experiments will show the similarity of this organism to treatment of patients with other nonspecific protein. The ease with which the organism has been discovered recalls the experience several years ago when the scarlet fever streptococcus was cultured so easily from the throat of patients suffering from the disease. These methods have been tried previously without success in rheumatic fever. If the organism discovered by the author can be constantly recovered and has the ability of producing an antiserum in animals, that will cure the infection in human beings, this discovery is of great importance.

Stewart, Harold J., and Crawford, J. Hamilton: The Effect of Tachycardia on the Blood Flow in Dogs. I. The Effect of Rapid Irregular Rhythms as Seen in Auricular Fibrillation. II. The Effect of Rapid Regular Rhythm. Jour. Clin. Inves., 1926, iii, 435 and 449.

I. The authors have studied the effect of auricular fibrillation on the blood flow in ten dogs. Two additional experiments serve as controls. The results of these experiments indicate that the blood flow is decreased during auricular fibrillation from 20 to 62 per cent. The oxygen saturation of the arterial blood was unchanged while that of the mixed venous blood decreased. Following the return of the heart to the normal rhythm, the oxygen saturation of the mixed venous blood and the blood flow returned to normal. In one instance in which spontaneous auricular fibrillation persisted there was no such tendency.

The authors conclude therefore that the heart during auricular fibrillation is less effective in the propulsion of blood than it is during normal slow rhythm.

II. The blood flow has been studied during artificially induced regular tachycardia in normal unanesthetized dogs. It was found that during regular tachycardia the blood flow was usually unchanged but in one-third of the observations it was decreased. During the regular tachycardia the oxygen saturation of the arterial blood was usually unchanged but a small decrease of 4.7 per cent occurred in one-third of the observations. In five experiments the effect of regular tachycardia and auricular fibrillation of the same or comparable ventricular leads was compared in the same dogs. The blood flow was decreased as usual during auricular fibrilla-

tion while in regular tachycardia the blood flow was unchanged except in one observation. The authors conclude that it is possible for the heart to be as efficient in the propulsion of blood during regular tachycardia as during the normal slower rhythm. Tachycardia, per se, does not produce anoxemia of the arterial blood. Irregular tachycardia does not affect the oxygen saturation of the arterial blood. Regular tachycardia may occasionally be followed by a slight decrease in arterial oxygen saturation.

Hewlett, A. W., Barnett, G. D., Lewis, J. K.: The Effect of Breathing Oxygen Enriched Air during Exercise upon Pulmonary Ventilation and upon the Lactic Acid Content of the Blood and Urine. Jour. Clin. Inves., 1926, iii, 317.

In the following investigation the subjects performed measured exercises and the effect of breathing oxygen enriched air upon the lactic acid content of the blood and urine was studied.

Method: Exercise was performed on a treadmill, the steps of which were 7 inches high. The rate was such that approximately 85 to 90 steps were ascended per minute. The amount of work performed was varied either by altering the duration of the exercise or by having the subject carry a load of 30 to 45 pounds. During the exercise the subject breathed through a rubber mouthpiece with the nose closed. Expired air was collected in Douglas bags. Minute collections were made and the minute volumes later determined. Urine was collected for a period of one-half to one hour before the exercise and for a period of approximately one hour after the exercise. Blood was drawn from the arm vein immediately before the exercise and again about four minutes after the exercise.

A slower rise of blood lactic acid and a slower excretion of lactic acid were found when oxygen enriched air was breathed. Excess excretion of lactic acid of the resting level was only demonstrated in experiments in which the blood lactic acid rose to 30 to 40 mg. per 100 c.c.

Starr, Isaac, Jr., and Gamble, Clarence James: A Method for the Determination of Minute Amounts of Ethyl Iodide in Air, Water and Blood by Means of Its Reaction with Silver Nitrate; and Experiments Bearing on the Determination of Blood Flow by Means of Ethyl Iodide. Jour. Biol. Chem., 1927, lxxi, 509.

This study was undertaken as a result of certain observations made by the authors which cast doubt on the validity of the ethyl iodide method of determining the circulation rate. The points in question were: (1) The accuracy of the iodine pentoxide train in the analysis of the ethyl iodide. (2) The coefficient of distribution of the ethyl iodide in the blood. (3) The rate of destruction of ethyl iodide in the body.

The iodine pentoxide method for analysis was found to give low figures as the rapid flow through the pentoxide pulled through part of the ethyl iodide and changed. A new micro-method for the determination of ethyl iodide in the air and blood was therefore devised. The specimen of blood was boiled in a vacuum and the ethyl iodide caught in a large tube. Standard silver nitrate in nitric acid was added to the tube containing the distillate. The reaction was completed after twenty-four to forty-eight hours and the excess of silver nitrate was determined according to the Volhard principle.

The coefficient of distribution of ethyl iodide in air and blood was also determined. Ethyl iodide vapor was introduced at the rate of 2 liters per minute into a tonometer containing distilled water. At intervals the flow was stopped and samples removed for analysis. It was found that the distribution coefficient was 2.7 in water. Similar experiments were done with human blood treated with oxalate

or fluoride, when it was found that the distribution coefficient was 7.6 instead of 2.0, the previously accepted figure.

The rate of destruction of ethyl iodide in the blood and its elimination by the lungs was also determined. The authors found it to be a slow, rather than a rapid process, ethyl iodide being detected in the alveolar and expired air after breathing. The error involved invalidated the ethyl iodide method completely though it was thought that a correction could be made, if one knew the concentration of ethyl iodide in the mixed venous blood within thirty seconds of turning off the ethyl iodide. This is impossible (1) because within thirty seconds the circulation has reached the lungs a second time and (2) it may take more than thirty seconds for equilibrium to be established. The authors consider that the blood flow figures obtained by the ethyl iodide method only approach those obtained by other methods because two errors are involved which tend to cancel one another.

Stewart, Harold J.: The Effect of Increased Heart Rate Due to the Injection of Atropine on the Oxygen Saturation of Arterial and Venous Blood of Patients with Heart Disease. Jour. Clin. Invcs., 1926, iii, 241.

The present study was undertaken in an attempt to contribute to the solution of the problem of the effect of rapid heart rate on the oxygen saturation of the arterial blood. There were six observations in five patients with auricular fibrillation and four in patients with normal rhythm. In one of these similar observations were made also during the presence of auricular fibrillation. The results of these observations may be summarized as follows: (A) in patients with heart disease tachycardia, per se, with either regular or irregular rhythm does not change the degree of arterial oxygen saturation; (B) during the time of rapid rate the degree of venous oxygen saturation is (1) unchanged in cases of valvular disease (other than mitral stenosis) irrespective of rhythm, (2) increased (a) in mitral stenosis if auricular fibrillation is present and (b) with undamaged valves when normal rhythm is present, (3) decreased in mitral stenosis if normal rhythm is present.

The plan of the study was to observe the oxygen saturation during the period of slow cardiac rate and shortly afterward during a period of most rapid rate. The rapid rate was produced by the injection of atropine sulphate intravenously. Samples of arterial blood were taken from a radial or brachial artery and samples of venous blood without stasis from a cubital vein.

Campbell, J. M. H.: Effect of Exercise on the Respiratory Exchange in Heart Disease. Guy's Hospital Reports, Oct., 1926, lxxvi, 394.

Twenty patients with varying types of heart disease were investigated from the standpoint of their reaction to exercise. The standard exercise consisted in stepping on and off a 13 inch block 12 times a minute. The total duration of the exercise varied from one to three minutes. Observations were made on the pulmonary ventilation, the oxygen consumption, the vital capacity and rate of breathing.

Comparing the breathing at rest in the normal subjects and in the cardiacs, it was found that in the latter group the ventilation was considerably increased, the increase being greater in those with aortic lesions and in those who were more severely ill. After exercise cardiac patients of all types showed a delay in the return of the ventilation to normal. One minute after a three minute exercise the ventilation in the normal individual had fallen 26 per cent and after five minutes the increase above the resting value was less than 5 per cent. Cardiacs, on the other hand, showed a decrease of only 10 per cent in the first minute after exercise and after five minutes their ventilation was still 25 per cent above the resting value.

The greatest increase in pulmonary ventilation after exercise was shown by the normal subject and this holds true, especially in the first minute. Patients with aortic disease, however, seem to show a greater increase but this was more apparent than real and was due to their higher resting value.

The depth of breathing at rest and after exercise was also studied. Aortic cases showed deeper breathing at rest and, after exercise, in spite of the increased rate, the breathing became even deeper. Patients with mitral disease, on the other hand, showed a shallow breathing at rest and after exercise breathing was rapid and the vital capacity much more diminished than in the aortic cases.

The oxygen consumption in cardiac patients at rest did not vary greatly from the normal. The amount of oxygen consumed after exercise was greater in cardiacs than in normal subjects and the former class was no greater than in the controls. In other words, cardiacs use more oxygen for the same amount of work and do not obtain the same proportion that they require during the exercise itself, but continue to consume more after exercise is finished. The dyspnea is thus due to their diminished ability to increase ventilation and oxygen consumption. These factors would be inadequate to produce dyspnea in the normal subject.

Smillie, W. G., and Augustein, D. L.: Vital Capacity of the Negro Race. Jour. Am. Med. Assn., 1926, lxxxvii, 2055.

This study of the vital capacity of negroes is a by-product of a hookworm study in a group of about 2,000 white and negro children of school age in southern Alabama One of the measurements used in the determinations of the physical condition of these children was vital capacity. The authors were surprised that normal negro children had markedly lower vital capacity than white children of the same age, sex and economic status. When calculated from surface area, the difference is from 15 to 20 per cent in children and from 25 to 35 per cent in adults.

The growth curves of weight and of standing height of white and negro children corresponds closely, but the negroes have a shorter trunk length than whites. When vital capacity is calculated from stem length, therefore, there is less discrepancy between the vital capacity of the two races than when it is calculated from surface area or standing height, the results being only 10 to 15 per cent lower than in the whites.

Christian, Henry A.: Speculation on Some Problems of Cardiac Failure. South. Med. Jour., 1927, xx, 28.

The author presents a picture of patients having chronic myocardial failure and describes difficulties they present in care and treatment. Two points stand out with great prominence in these cases. During life the heart obviously has failed to function and after death it gives every appearance of being an unusually powerful organ. Certain variants are frequently encountered in these patients. There may be hypertension or arteriosclerosis or albuminuria and the heart muscle at autopsy shows fatty degeneration and patches of fibrosis. All or any of these findings may be encountered in a just detectable stage or, at other times, a marked degree.

The author discusses clearly and at length the so-called work-hypothesis of heart hypertrophy. He also discusses the influence that infection or other toxic processes may have in causing the degenerative changes in the heart muscle. He points out that in our lack of exact knowledge of the cause and mechanism of cardiac hypertrophy and failure, the clinician must still rely much on his individual experience acquired in the careful observation of his own patients.

Roddis, L. H., and Cooper, G. W.: Effect of Climate on the Blood Pressure. Jour. Am. Med. Assn., 1926, lxxxvii, 2053.

The authors studied the blood pressures of a group of naval officers on board ship on West Indian waters. They found that in the tropics systolic blood pressure of normal white males varies 10 to 15 mm. mercury below the normal for the temperate zone. The change is not a rapid one and represents a lower vasomotor tone and a general slowing of physiological activity.

The routine of life must be modified to suit this alteration of physiological activity, if injury to the health is to be prevented. This change is the mode of life including limiting regular work to the cooler part of the day, avoiding excessive physical exertion, the adoption of the siesta and observing precautions as to food and clothing. The blood pressure and basal metabolism being affected by climate, it is probable that variations in other physiological processes occur and should be investigated.

Bunderson, H. N., and Falk, I. S.: Low Temperature, High Barometer and Sudden Death. Jour. Am. Med. Assn., 1926, lxxxvii, 1987.

The authors have arranged a series of curves to show the seasonal variations in mortality from organic disease of the heart or from organic diseases of the heart, cerebral hemorrhage or chronic nephritis combined in mean weekly temperatures and in mean weekly barometrical pressures. The data were derived from the records of the vital and weather statistics of Chicago for the period January, 1924 to April, 1926. The curves show that mortality was high when temperature was low and vice versa. There is no clear apparent correlation between fluctuations in mortality and in barometrical pressures.

Variations in mortality from the specified causes are inversely correlated to a very high degree with variations in temperature in the second and fourth, but not in the first and third quarter of the year. The results of this investigation suggest that patients who are especially exposed to the lethol effects of organic diseases of the heart, cerebral hemorrhage and the chronic nephritis should be warned of the unusual danger attendant on cold weather.

Marvin, H. M.: The Value of Xanthein Diuretics in Congestive Heart Failure. Jour. Am. Med. Assn., 1926, lxxxvii, 2043.

A group of 77 adult patients with advanced congestive heart failure were treated with digitalis and diuretics of the xanthein group. Theophyllin, theobromin and theobromin sodiosalicylate.

Thirty-six were made edema free by digitalis alone; 13, of the remaining 41, were entirely relieved of edema by one or more of the diuretics employed; 5 others had well marked diuresis with loss of most of the edema and 5 were moderately benefited.

Theobromin sodiosalicylate in doses 2.6 to 5.3 gm. daily for five to six consecutive days was effective in only 2 of 8 patients. Although 5 of the remaining 6 responded satisfactorily to theobromin and theophyllin, it was regarded as of very little value.

Theobromin in doses of 0.6 gm. three times a day for two days was partially or entirely satisfactory in 7 of 17 patients. Of the remaining 10, one-half later obtained excellent diuresis from theophyllin. Theobromin was a far more effective diuretic than was theobromin sodiosalicylate and was equally devoid of undesirable side actions.

Theophyllin was far more potent of the three preparations. It proved effective in a number of persons who had failed to show diuresis after the administration

of other drugs. Its therapeutic usefulness was somewhat limited by the nausea and vomiting that followed its use.

There seems to be no sound basis for the attitude assumed by many that diuretics are worthless. A certain proportion of cardiac patients can be relieved of symptoms by these drugs if adequate treatment with digitalis has completely failed. It is evidence to indicate that the xanthein diuretics are more effective in the arteriosclerotic hypertensive heart disease group as contrasted with the rheumatic heart disease group.

Gold, Harry: Tolerance for Digitalis in Experimental Diphtheria. Jour. Am. Med. Assn., 1926, lxxxvii, 2047.

The author has carried out fifty experiments on the cat to determine the effect of digitalis and diphtheria toxin on the heart muscle. The present study shows that there is no direct synergism between diphtheria toxin and digitalis even though the heart has been sufficiently injured by the toxin and that diphtheria toxin does not diminish the tolerance of an animal to digitalis unless that animal has been reduced to a state of extreme circulatory depression or collapse.

There are clinical conditions in which patients become more susceptible to the digitalis bodies. It has been frequently seen that some patients with heart disease in the terminal stages become extremely susceptible to the toxic action of digitalis. It is doubtful, however, whether the increased susceptibility observed in nearly moribund animals has any important bearing on the clinical problem or the use of digitalis in patients with diphtheria. The experimental work does justify the expectation that in certain cases of circulatory disturbances produced by diphtheria, digitalis in the proper dosage would be of value.

Holman, Emile, and Beck, Claude S.: The Physiological Response of the Circulatory System to Experimental Alterations. III. The Effect of Aortic and Pulmonic Stenoses. Jour. Clin. Inves., 1926, iii, 283.

The following study was undertaken to determine the effect of altering the flow through the heart by introducing into the circulatory system pulmonic stenosis or aortic stenosis and to compare the effect of such stenoses with the effect of a defect in the interventricular septum. It may be considered that the effect of such stenoses is to impede the flow of blood through the circulatory system by increasing the peripheral resistance against which the right and left ventricles perform their work, while the effect of the septal defect is to increase the flow of blood through the heart.

The hearts of dogs were exposed at operation under aseptic precautions. Stenoses of the aorta and pulmonary arteries were produced by placing around the vessel a constricting band of tape or aluminum. Interventricular fistulae were produced by incising the septum with a long slender knife inserted through the left ventricle. During the period of observation the pulse rate and the presence of thrills and murmurs were noted. The volume of the circulating blood was determined by the intravenous injection of brilliant vitol red. Changes in the size of the heart were determined by roentgenograms and at autopsy the heart was measured and the cardiac muscle was studied histologically.

Certain observations in the protocols may be emphasized. A stenosis which permanently constricted the pulmonary artery to a circumference less than one-half the normal size was invariably fatal. A pulmonic stenosis of marked degree was immediately followed by an acceleration in pulse rate and by a drop in general blood pressure, both of which gradually approximated normal. The recovery of blood pressure was more rapid in the presence of a pulmonic stenosis than in the

presence of a large interventricular septal defect. The stenosis was followed immediately by a dilatation of the right ventricle, a dilatation which gradually subsided during the subsequent months until the heart again assumed a normal size as shown by roentgenographical studies. At necropsy a slight thickening of the right ventricular wall was found in one instance, as previously observed by Reid. Microscopically, the right heart showed evidence of hypertrophy definitely more marked than in the left heart. The slight effect of a pulmonic stenosis of this duration upon the size and thickness of the right ventricle was a marked contrast to the pronounced effect of a large interventricular defect of equal duration as observed in a previous study. The latter was followed by a conspicuous dilatation and thickening of the wall of the right heart. There was no demonstrable increase in total blood volume after pulmonic stenosis such as developed in the presence of interventricular defects.

The production of the pulmonic stenosis resulted in a well marked systolic bruit followed by an accentuated pulmonic second sound. A thrill was felt at the time of operation limited to the vessel beyond the stenosis. It could not be felt by palpation of the chest wall, whereas the septal defect invariably produced a pronounced thrill palpable over the chest wall.

The establishment of an interventricular septal defect some days after the production of a pulmonic stenosis in the same animal resulted, when the animal survived, in a relatively much greater enlargement of the heart from the septal defect, as compared to the slight enlargement which followed the production of the pulmonic stenosis alone. This enlargement of the heart is due almost entirely to dilatation rather than to hypertrophy. It may be inferred, therefore, that an increase volume flow through the right heart resulting from a septal defect is a more effective means of producing right sided cardiac enlargement than is the increased peripheral resistance resulting from a pulmonic stenosis.

Additional evidence was also obtained indicating that in the presence of interventricular defects there is an increased flow of blood through the pulmonary circulation and that this may be diminished by producing in the same animal a pulmonic stenosis. In two of the experiments the animals survived large septal defects when associated with a pulmonic stenosis, whereas interventricular defects of equal or of smaller size in other animals proved invariably fatal due to pulmonary congestion and edema. That this pulmonary congestion and edema which accompanies excessively large interventricular defects may be the important factor in the death of these animals was indicated by the turn of events in one experiment following erosion of the constricting tape through the pulmonary artery. This erosion permitted an increased flow through the pulmonary circuit producing marked congestion and edema of the lungs which proved fatal.

Aortic stenosis beyond the left subclavian artery lowered peripheral blood pressure but caused no acceleration in pulse. Such a stenosis not only lowered femoral pressure but increased carotid pressure. Well marked aortic stenosis of six months' duration produced no roentgenographical increase in the size of the heart, and at necropsy there was no apparent dilatation of the heart, but a slight increase in thickness of the left ventricular wall, which microscopically showed a slight hypertrophy.

An instructive comparison may be made between the first experiment, in which an aortic stenosis of six months' duration was produced, and an experiment already published, in which a large septal defect of eight months' duration had been produced. These animals were of the same breed and weight, but at necropsy the heart of the former animal weighed 165 gm. whereas the heart of the latter animal weighed 226 gm. It is quite evident that the septal defect with its resulting increased flow of blood through the heart produced a much greater hypertrophy of

the cardiac muscle than did an aortic stenosis sufficient to cause a permanent lowering of the peripheral femoral pressure. The authors infer, therefore, that an increased flow of blood through the heart is a more effective stimulus to cardiac dilatation and hypertrophy than increased peripheral resistance. The total blood volume remained relatively unchanged in the presence of an aortic stenosis. The production of an aortic stenosis was followed by a systolic bruit heard best along the left vertebral border. There was no palpable thrill.

Certain other differences may be noted in the effects produced by large interventricular septal lesions as compared to the effect of a pulmonic or aortic stenosis. In the former there were invariably microscopical and macroscopical evidences of pulmonary congestion and edema. In the latter these were not consistently observed either macroscopically or microscopically, and in most of the cases of uncomplicated pulmonic stenosis a marked emphysema was noted. In those animals with an aortic stenosis in which a sudden exsanguination occurred through erosion of the vessel wall there was also microscopical emphysema of the lungs. Respirations were more rapid in the presence of an increased flow through the lungs as produced by interventricular defects than in the presence of a pulmonic stenosis.

It is evident also that, roentgenographically, a marked enlargement of the heart usually indicates dilatation. Hypertrophy, if it exists, produces little evidence of its presence by the roentgenograms. One may infer, therefore, that any great increase in the size of the heart observed clinically is in greater part due to dilatation and in lesser degree to hypertrophy.

Partial constriction of the pulmonary artery or aorta by a metal band or tape frequently ended fatally through erosion of the vessel wall.

Brown, Samuel and Weiss, H. B.: Lateral Views of the Heart and Aorta. Jour. Am. Med. Assn., 1927, lxxxviii, 226.

During the last two years the authors have made a study of the heart and aorta and their relation to the thorax in the lateral view. A study of several hundred roentgenograms of thoraces of normal and abnormal persons yielded the information presented here.

1. In the lateral view of the thorax the heart is seen to be placed obliquely. The apex of the heart is directed downward and forward and the base is directed upward and backward. Under normal conditions it has been observed that the lower portion of the anterior border of the heart is in contact with the anterior wall of the chest which corresponds on percussion to the area of superficial dulness.

2. In the lateral view the configuration of the heart shadow is oval. The upper pole points upward and backward and corresponds to the arch of the aorta. The individual chambers of the heart can be outlined by drawing a line between the two poles. This line divides the heart into approximately two equal parts; the anterior half corresponds to the so-called right side of the heart and the posterior half corresponds to the so-called left side of the heart. A line drawn at right angles to the median line midway between the poles will approximately divide the ventricles below from the auricles and aorta above. With a knowledge of the relative position of the chambers, changes in size of any one of them can be determined to a large degree.

3. Under normal conditions the heart will be found to be situated in the anterior half of the thorax. In marked enlargement, the posterior border of the heart may even reach the dorsal vertebrae.

4. The oblique position of the heart in the lateral view of the thorax forms two transparent triangles. One is located above and in front of the anterior surface of the heart and large blood vessels. The other is located in the retrocardiac space and is called the posterior inferior triangle.

5. The lateral view lends itself readily to a more thorough examination of the aorta by eliminating to a large degree the overlapping and superposition of the various structures.

The authors describe their technic for making the films.

Hare, Hobart A.: Wiring with Electrolysis in Saccular Aneurysm. Jour. Am. Med. Assn., 1927, lxxxviii, 230.

In this article the author reports two additional cases of aneurysm of the thoracic aorta treated by wiring with electrolysis and in addition makes note of 19 points in the technic of the procedure. As a result of 36 such operations a number of points have arisen which deserve emphasis, the more so because at various times cases have been referred which were not suitable for the wiring operation and instances have been reported in which failure occurred because of error in technic.

White, Paul D.: A Note on the Differentiation of the Diastolic Murmur of Aortic Regurgitation and of Mitral Stenosis. Boston Med. and Surg. Jour., 1926, cxcv, 1146.

The author gives a brief description of three murmurs heard in these conditions which are sometimes confusing. Their differential diagnosis is discussed. He also offers a table pointing out the differences between the signs of aortic regurgitation and mitral stenosis. In the former the murmur occurs early, immediately following the second sound; it is blowing, often high pitched. It is maximal along the left border of the sternum heard frequently at the apex and rarely maximal in the aortic area. It is best heard in the upright position as a rule and with the chest leaning forward. The murmur is best heard with the flat chest piece with diaphragm. Sometimes it may be heard better with the naked ear.

The murmurs of mitral stenosis occur later, beginning an appreciable interval after the second sound, often immediately after the third sound when it is present. It extends through middiastole if loud. If the stenosis is well marked and the rhythm normal, it is followed by a presystolic accentuation and thrill, especially when the pulse is quickened after exercise. It is rumbling in character, usually low pitched, rarely blowing. It is maximal at the apex and often limited to a very small area but sometimes heard as far as the sternum. It is best heard in the recumbent position and with the bell chest piece.

The Austin Flint murmur is exactly the same in all characteristics as the diastolic murmur of organic rheumatic mitral stenosis. It can be differentiated only by postmortem examination or by exclusion of the probability of disease of the mitral valve.

Levine, Samuel A.: The Treatment of Attacks of Syncope Occurring in Adams-Stokes Disease. Boston Med. and Surg. Jour., 1926, cxcv, 1147.

In the treatment of patients suffering from Adams-Stokes Disease, a specific treatment of the syncopal attacks presents a distinct problem apart from whether or not there is congestive heart failure. Often these attacks are fatal in patients who have been ambulatory and have been maintaining a satisfactory circulation. The author reports a case showing that during the long attacks of asystole of the heart, that occur with unconscious periods, adrenalin chloride where injected directly into the heart was life-saving. It is obvious that at the moment when there is no circulation, intramuscular or even intravenous injections would be useless. It is true, however, that if a patient recovers there is a period of a few hours following

intramuscular adrenalin injections during which he may be free from attacks, although it is no indication that adrenalin itself prevents the return of attacks.

Recent experience with the oral administration of barium chloride indicates that it is very valuable in actually preventing recurrences and the successes warrant a further trial of this medication when attacks of syncope are frequent.

Eakin, W. W.: Paroxysmal Tachycardia. Can. Med. Assn. Jour., 1926, xvi, 1454.

The author reports five cases of paroxysmal tachycardia.

Case 1 was auricular in nature and showed a change of the electric axis when recovery took place.

Case 2 was auricular in nature in a man thirty-one years old. A tachycardia was followed by normal rhythm and later by auricular fibrillation. The author points out in this connection that the presence of auricular extrasystoles, auricular tachycardia and fibrillation in the same case has suggested a common etiological factor and attention has been drawn to the possibility that the extrasystoles and tachycardia may also be due to a circus movement.

Case 3 showed an irregular ventricular tachycardia developing in a case in which the myocardium had already been considerably damaged. The patient was thirteen years of age.

Case 4 showed a ventricular tachycardia with intermittent attacks for as long as the patient could remember. The patient was fourteen years old. Few other symptoms were present and there was apparently little myocardial damage.

Case 5 showed a ventricular tachycardia occurring with severe acidosis.

Clerc, A. and Levy, R.: Ventricular Anarchy. Presse méd., Aug. 25, 1926.

The authors describe a form of ventricular arrhythmia which occupies a position between the irregular ventricular rhythm which accompanies auricular fibrillation and actual ventricular fibrillation. To this arrhythmia they give the name "ventricular anarchy." The auricles appear to be in a state of fibrillation and the ventricular beats are irregularly spaced and seem to have multiple foci of origin which are constantly shifting. Six observations are recorded. The rhythm is extremely variable and may be quasi-normal, slow, rapid or irregular by turns. The arrhythmia is not necessarily progressive and may appear in attacks. The atypical and variable character of the form of the ventricular complexes baffles description. Similar curves are seen experimentally in animals during the course of profound intoxications by digitalis, strophanthin, cinchonine, etc., and following ligation of the coronary arteries. The prognosis is very grave, death having occurred in the authors' series within a few weeks or months or at the most at the end of a year. Digitalis is not responsible for the production of this abnormal rhythm, but in its presence should be used with the greatest caution.

Book Reviews

ARTERIOSCLEROSIS AND ITS TREATMENT.—By Prof. G. Galli. Societa Editria Libraria, Rome, Milan, and Naples, 1926. Pp. 476.

Dedicated to the memory of G. Bacelli and C. Gerhardt in whose service the book took its origin, this treatise is based upon the personal experience of the author, substantiated by the numerous works which he had already devoted to the subject. After establishing in the initial sections the anatomical, anatomical-physiological, etiological and historical foundations of the problem, and setting forth the demographic relations, Galli systematically reviews in a series of chapters the principal clinical aspects. Arteriosclerosis of the brain, cord and bulb are successively considered, with reflections upon central motor paralyses of vasomotor and organic origin. Special attention is paid to arteriosclerosis of the heart and the reader will find an exposition not only of the relations between sclerosis of the myocardium and coronary ischemia, but also a long discussion of the relation of the latter to angina pectoris. The anatomical theory supplemented by that of vascular spasm appears to be the most appropriate. Mention should also be made of the chapters devoted to arteriosclerosis of the aorta, pulmonary artery and the large abdominal arteries. The chapter on the kidney includes a critical examination of the diverse causes of hypertension. Several pages upon arterial disease of the limbs and peripheral territories terminate the third section. The fourth section which is devoted to therapy consists of fully 100 pages, and contains the most recent information concerning the use of drugs, physical agents and general and alimentary hygiene.

This, then very imperfectly reviewed, is Galli's work, a book which is remarkable not only for its wealth of personal documentation which is illustrated by diagrams, figures (many of which are colored) and photographs, but also for the precision of the bibliographical references. Moreover due mention must be made of the author's expository style which reveals at once a careful anatomist, a sagacious clinician and a man of letters (see for instance the chapter on the history of angina pectoris). The specialist as well as the practitioner will derive both profit and pleasure in reading these attractive pages. Let us hope with the author that they contribute to the understanding and prophylaxis of a pathological condition which because of its great frequency and world-wide distribution constitutes a veritable scourge of modern life.

A. CLERC.

LE RHUMATISME ARTICULAIRE AIGU MALADIE CONTAGIEUSE ETUDE EPIDEMIOLOGIE ET PATHOGENIGAL.—By Doctor Georges Andrieu. Imprimierie J. Fournier, 41 rue Constantine, Toulouse, 1926. Pp. 142.

The thesis here presented, while not entirely new to American students of preventive medicine because of the contributions of St. Lawrence, White, Abeloff, and Sobel and others in recent years, is sustained by material much more convincing than any heretofore published.

The chapters dealing with the geographical distribution of acute articular rheumatism and the contributory causes, while admirably prefaced and giving a good deal of hitherto inaccessible material particularly from French military sources, do not add much to our ideas and accepted understanding of the disease.

The third chapter, however, upon the epidemiology of acute rheumatic fever, contains valuable, new, and convincing matter.

Dr. Andrieu's description of the rural epidemic in and about Aucun in 1925-1926 and his history of an outbreak in the garrison troops at Toulouse 1924-1925 are useful, original observations which, taken with the presumptive evidence of secondary cases in homes of clinic patients so generally found in cities of this country tend to confirm the steadily growing opinion that in acute rheumatism we are dealing with a communicable disease transmitted by human contact or exposure to discharges of persons sick with the disease.

Hardly more can be done or planned for prevention than to act on general principles until the etiological agent has been determined. Andrieu makes no claims of discovery in this field.

Dr. Andrieu finds that: relatively long and intimate contact between the sick and the well is necessary for transmission of the infection; the contagium is only by interhuman contact; that the incubation period is still undetermined; that abortive forms are common; that there are convalescent and recurrent carriers of the virus; that immunity is not developed by an attack of acute rheumatic fever.

In the closing chapter on prevention Andrieu refers to the presumed contributory factors of poverty, overcrowding of living premises, including the effects of dampness, cold and fatigue, and to the still controversial rôle of focal infection as in teeth and tonsils.

Personal or family prophylaxis should include isolation of the sick from the well and concurrent disinfection of oral discharges coupled with disinfection (sic) of the rhinopharynx.

It is rare to find in a thesis from French authorship so generous a collection of references to medical publications from England, Germany and this country.

This publication should be of interest to all those who concern themselves with the natural history and prevention of valvular heart disease, and to those who seriously study the end-results of operative removal of foci of infection in teeth and tonsils. It presents an all too rare approach to a disease from a broad epidemiological point of view.

H. E.